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Contents

The Status and Development of Biophysics: *Ralph W. Stacy* 169

Technical Papers

The Physiologic Limits of Vision: *Elizabeth W. Olmsted* and *Elizabeth P. Olmsted* 176

Intracellular Localization and Distribution of Carbonic Anhydrase in Plants: *E. R. Waygood* and *K. A. Clendenning* 177

Animal Protein Factor in Crude Casein and its Vitamin B_{12} Relationships: *M. Piccioni, A. Rabbi,* and *G. Moruzzi* 179

A Micro Ball Mill for the Disintegration of Bacteria: *Carl-Göran Hedén* 181

The Purine and Pyrimidine Content of Three Strains of *Escherichia coli*: *A. Marshak* 181

A Simplified Technique for Microelectrocoagulation: *Mychyle W. Johnson* and *L. J. Manhoff, Jr.* 182

Glycogen Storage in the Heart in Experimental Renal Hypertension in the Rat: *Robert W. Lackey* 184

The Direction of Flow in Blood Vessels of the Infundibular Stalk: *R. J. Barrnett* and *R. O. Greep* 185

A Universal Line Graph for Estimating Percentage Potency in Multidose Assays: *Marion B. Sherwood* 185

Potassium Excretion in Rats: *S. E. Dicker* 187

Silver Nitrate as a Test for Ortho and Para Dihydric Phenols: *Bernard S. Wildi* 188

Comments and Communications

Dr. Langmuir's Article on Precipitation Control: Discussions by *Ferguson Hall; Gardner Emmons, Bernhard Haurwitz, George P. Wadsworth,* and *Hurd C. Willett* 189

Scientific Book Register 192

News and Notes 193

Industrial Noise 3

Meetings & Conferences 12

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Industrial Noise

As a result of increasing activity by insurance companies and otologists, interest in both the limits of safety and the means whereby noise levels can be kept below the safe limits is growing, although it has not yet been reflected in an increase in articles in scientific journals. Under the sponsorship of the Navy, data were sought on the character of the actual shop environment and its influence on industrial workers as revealed in the statistical analysis of individual audiometric records. MacLaren and Chaney did the audiometric work, and Veneklasen did the environmental survey work at Lockheed's Plant in Burbank, California. The uniqueness of this study lies in the fact that it drew its data from the actual working environment and from the people who worked in it; its significance is that it is rapidly becoming the model that other industrial studies are following. The pilot plant research program recommended by the American Academy of Ophthalmology and Otolaryngology is similar to the Lockheed study.

Contributing to the uniqueness of this study is its emphasis on the correlation between the manner in which effective pressure is distributed through the spectrum and the audiometric records, rather than on correlations between over-all levels and audiometric findings. Perlman's epoch-making generalization that "low frequency noise is less traumatic than high frequency noise" is being confirmed.

As these correlations become more clearly defined, limits of safety stated in terms of the effective pressure in the various parts of the noise spectrum will take the place of the present statements of limits in terms of the over-all levels. This, in turn, will restrict the number of areas that will be classified as "unsafe" and lead to more intelligent measures of noise reduction. Mathematical correlations between the environmental exposure expressed as a code and the audiometric result expressed as a code offer one of the most significant results to stem from the Lockheed study, although its authors do not indicate that they realized its possibilities.

Methods of using audiometers to test groups of people at one time are under study, according to publications by the Navy. The increased interest in spectrum analysis has caused increased interest in sound-level meters equipped with octave band filter sets and graphic recording instruments. Increased attention is also being given to quieting the machinery of production by individual concerns, but few data are available for publication. Reports from Armour Research Foundation and Penn State College give evidence of the increasing volume of activity in this field, although it cannot be said that the movement is widespread.

Members of the Acoustical Materials Association continue to search for better means of reducing injury and increasing comfort, with the result that acoustical materials tailored to fit the industrial environment are being announced. Noise abatement councils are renewing publicity drives aimed at more effective social control of noise. Scientific societies have become interested in setting up committees to keep the flow of information on industrial noise accurate; among them are the Council on Industrial Health of the American Medical Association, the Noise Abatement Committee of the Acoustical Society of America, and the Sub-Committee on Industrial Noise of the American Academy of Ophthalmology and Otolaryngology.

Relatively unexplored are the psychological effects of noise and the adverse effects of noise on labor turnover, absenteeism, quality of product, accident rate, and morale, largely because of the difficulty in showing these effects on the manufacturing cost sheet in dollars and cents. Confidence is expressed by research workers that, as the traumatic effect is stated more objectively, the intangible effects will be defined more objectively.

Ralph Martin McGrath
Acoustical Society of America

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The Status and Development of Biophysics

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IN THE PAST HUNDRED YEARS a number of text and reference books have been written on "biophysics." Each has contained that material which the author considered as biophysics, and each has differed from all the others. Some have been complete in one field, deficient in others; some have been inadequate in every field; and some have been so comprehensive that they have included much information rightly belonging to other disciplines. The definition of the field has varied from author to author, and it still varies. This lack of agreement on a definition has thus far hampered the development of biophysics as a field.

At present there are numerous agencies desirous of seeing such development proceed, and the near future should see a definition emerge. There are many excellent reasons for the currently surging interest in biophysics. Man now travels faster and farther, higher in the air, and deeper in the ocean, than ever before. He is exposed to new physical influences by virtue of the invention of new weapons and machines. We must learn the effects of these physical influences on living matter. Research in many biological areas has progressed to the point where physical analysis is imperative. The biologist is not equipped to perform complex physical analyses, and the physicist usually is not aware of the need for his ability, or he considers the problems unworthy of his attention. Physical instrumentation is becoming a discrete phase of biological experimentation, and the biologist alone cannot supply the needed apparatus. Therefore, a definite need for a significant number of well-trained biophysicists is indicated.

Modern physics is awe-inspiring to the general public, and perhaps to the biologist. It is even becoming common practice to frighten graduate students of the biological sciences by threatening to require advanced work in physics. There is an aura of mystery about the physicist, his apparatus, and his mathematical formulae. This mystery is a myth and is dispelled by familiarity. More and more biologists are learning physics because they are driven to it through specific needs. As they learn physics, they become thrilled by its prospects in biology. Like a new religion, biophysics is passed from one person to another, gathering converts in its progress. These converts are important to its continued existence.

Unfortunately, there is no uniformity in the approach of biologists interested in biophysics. Indeed, we do not even know what a biophysicist is! It is not a new science, for it has existed as long as the scientific method, though never as a separate science. Helmholtz, the greatest of all biophysicists, worked more than a hundred years ago, and no one will dispute his classification of his own work as biophysics. In the past, however, biophysics as a separate science has ventured timidly into the world, but has retreated into latency to await a more favorable opportunity. Now the stage seems to be set for its appearance. There is a growing demand for biophysicists; there are many excellent scientists interested in the subject, and the conditions existing in other biological sciences almost require its development into a special subfield. Laboratories of biophysics already exist in many of our leading universities and research institutions; some universities have new departments of biophysics, and courses in biophysics are being offered to biology and medical students.

Heretofore, the functions ascribed to biophysics have been performed by physiologists, bacteriologists, botanists, zoologists, physicians and, rarely, by physicists. To remove biophysics from these fields is a major amputation, for it constitutes a significant portion of some of them and, if it were severed from the rest of biology, it would lose its usefulness.

The heterogeneity among biophysicists does not admit of a uniform program of development for the field. There is almost a total lack of precedent in the training of biophysicists, for this has been haphazardly accomplished by many devious routes in the past. It is not surprising, then, that those concerned with the development of biophysics as a field of endeavor are beset with problems. Some of these problems have seemed almost insurmountable and have been responsible for the failure of the field to emerge in previous times. Among the major questions are the following:

1. What should be the scope of biophysics?
2. Should the subject be organized as a separate field, or as a subdivision of biology or physics?
3. From what personnel sources should students be recruited?
4. What constitutes an adequate curriculum?
5. How can biophysicists be most useful to society?

These questions cannot be answered singly, for each has a bearing on the others. This discussion will present possible solutions. The thoughts set down herein are of necessity preliminary, for actual practice may indicate the need for appreciable revision. It is the purpose of this paper to precipitate interest by supplying a definition of biophysics and proposing a detailed program for the training of biophysicists. It is hoped that other, more profound and practical analyses of the situation will be born of this beginning.

Current Views of Biophysics

Loofbourow (1950), in a calm and objective analysis of biophysics, has subdivided the field into three main divisions; namely, the physics of biological systems, the biologic effects of physical agents, and the use of physical methods in the study of biologic problems. This is a correct definition in that it is sufficiently broad to encompass whatever one might wish to include in it, but it is not specific enough to be of use in planning the development of the field.

The greatest of the printed works on biophysics is the magnificent reference edited by Otto Glasser (1944, 1950). Its two volumes, some 3,000 pages in length, contain authoritative articles on virtually every subject that might be considered biophysics. Glasser belongs to a school of thought (with which I agree) that includes in biophysics the thorough study of all the physical phenomena used by the biologist to study or explain the behavior of living matter. (This concept will be discussed in detail later.)

To a very large number of scientists, biophysics means the application of nuclear physics to biology. The *Advances in Medical Physics* (1948) and *Symposium on Applied Biophysics* (1949) are devoted almost entirely to this type of information, although this viewpoint is not adequate from the long-range standpoint.

A third group would limit biophysics to the study of the physical nature of protoplasm and cells, including such phenomena as viscosity; coagulation, gelation, and thixotropy; elasticity of protoplasm, permeability of membranes, and so on. They call these the "fundamentals" of biology, and in their eyes biophysics should be limited to such studies.

We may recognize a fourth (and unfortunately large) group that looks on biophysics as the process of furnishing instruments for use by biologists and on the biophysicist as a gadgeteer. This is sheer sacrilege to a true lover of the subject, and the danger of this attitude cannot be overemphasized.

A fifth group, with fewer disciples than most fields (for obvious reasons), embraces the mathematical approach to solutions of biological problems. It has been stated, facetiously, to be sure, that young and eager scientists often take courses in the calculus and from that time on consider themselves "biophysicists." This is not so deplorable as it may seem, for these young specialists have become aware of a gap in their training and are striving to fill it. Admittedly, they are rushing the issue, for they have only a glimpse of a vast and complex vista of work to be done.

Still other groups lay greater or less claim to biophysics but, obviously, no concerted effort toward development of the field can be made until there is widespread agreement as to what shall constitute the field. Each of the schools of thought listed above seems to be somewhat intolerant of the others' claims, and one of the cardinal needs for the future of biophysics is general agreement on a definition of the field.

I believe that the principal aims of the biophysicist must embrace the study of the physical analysis of biologic behavior, the determination of the effects of physical agents on biological material, and the application of physical techniques to biological measurement. Confining biophysics to one of the narrower fields of endeavor listed above would be like limiting biochemistry to the study of carbohydrates alone, or proteins, or lipids. Separation and development as a distinct field would not be appropriate within these narrower concepts, but with a broad definition of scope such separation is needed.

The Broad Concept of Biophysics

There is an impressive volume of material on living matter at the microscopic, submicroscopic, and molecular levels. This material is, of necessity, included in the broad definition of biophysics. The worker interested in this phase of biophysics would study tissue ultrastructure, especially with the aid of physical instruments, such as the electron microscope, the x-ray diffraction camera, the microscope centrifuge, and others. He would investigate the viscosity, elasticity, optical activity, surface activity, and numerous other facets of the behavior of protoplasm. He would look carefully at the physical nature of the environments in which living matter exists, and would study plant and animal material as a physical conglomerate in the midst of other physical systems.

The biophysicist must apply himself to the theoretical and experimental determination of the role of molecular and atomic structure in the production of physiological events. In spite of the increasing difficulty of application of theoretical physics (in view of the departure from classical Newtonian mechanics), the essential analyses will eventually be made, and the biophysicist will probably make them. In this respect, the biophysicist invades the domain of the physical chemist, but some such overlapping is inevitable. Biologists have, for the most part, ignored this fruitful field of research, but the future should see many profitable man-years spent in its pursuit.

With this introduction to the nature of physical biological existence, the biophysicist might proceed with the mechanics of living matter on a larger scale. He could analyze the motion of various parts of the body relative to each other, with special reference to force-torque relations of musculoskeletal systems. He could observe the effects of motion of the body through space, the effects of accelerations, such interesting factors as the mechanical impedance of living material, and the coefficients of elasticity and strength of materials making up biological matter. Such studies involve most of the fields of statics and mechanics and can, in fact, be used as an approach to the study of the physics involved. It is the author's understanding that a textbook of physics, designed expressly for premedical students and using this approach to the study of physics, is now in preparation.

The biophysicist must also turn to the applications

of heat physics to biology. He must know thermometry and calorimetry, and be able to analyze with precision phenomena involved in loss of heat from the body. He should scrutinize carefully the work of A. V. Hill, W. O. Fenn, and other famous biophysicists, on the production of heat in living matter, and he should carry further the investigations of the physical energetics of life. The thermodynamics of living matter constitutes a fundamental field of research that is rich in interesting and exciting biophysical problems.

The most obvious application of wave mechanics to biology is in the study of light and sound receptors. Here extreme care must be taken in the definition of the extent to which biophysics may go. One concept includes in biophysics all the physical phenomena occurring in the chain of receptive events up to and including the absorption of radiant and sonic energies, and their conversion to conducted disturbances. This seems a reasonable dividing point. This phase of biophysics also embraces the study of the effects of vibratory and radiant energies other than those of nuclear disintegration (which deserve separate consideration) on living material.

There are still many gaps in the understanding of electromagnetic spectra, from both physical and biological standpoints. The basic principles of particle analysis by spectroscopy have scarcely been applied to biology. Spectrophotometric analysis of biological materials, now limited almost entirely within or near the visible wavelength range, may constitute a real contribution to our knowledge of the primary nature of life. It is the biophysicist who will carry these analyses into the infrared, ultraviolet, short and long radio wave, x-ray, gamma, and cosmic regions. It is the biophysicist who will ultimately determine the pattern of molecular orientation that gives protoplasm the faculties of life, and he will do so through the fuller understanding made possible by new physical techniques.

There is no doubt that the electrical physics of living matter is of primary biophysical importance. The instrumentation necessary to measure bioelectric phenomena is essentially physical in nature, and analysis of the experiments performed in bioelectricity requires a thorough knowledge of the characteristics of the instruments used. Likewise, the production of potentials observed in living matter is at least partly physical and must be analyzed thoroughly with a view to physical interpretation, as has been done in the work of Kenneth Cole, Otto Schmitt, R. C. Beutner, and others. Only recently has there been consideration of the dynamic electrical characteristics of living tissues. The effects of passage of electric currents through animal and plant tissues invite investigation, and the application of electronics in instrumentation for study of phenomena other than bioelectric must be continued and enlarged.

The physics of gases has already been used in the development of protective devices for the aviator, in the diagnosis and treatment of respiratory diseases, and in increasing the ability of man to descend to great depths under the sea; and it may ultimately be considered in the development of space travel. At present, a full understanding of the dynamics of the respiratory system is rapidly becoming more attainable, thanks to the application of physics both in instrumentation and in theory.

Essentially the same is true of the application of fluid statics and kinetics to biology. For the most part, this application has been concerned with the study of circulation of blood in large animals, under the names "hemostatics" and "hemodynamics." The biophysics of circulation includes the study of pressure-flow relations, the energy content of the blood under different conditions of pressure, velocity, and position. It involves the analysis of factors contributing to the resistance of blood flow through tissues, the occurrence of turbulence, and the application of Poiseuelli's equations, Bernouilli's theorem, etc.

The biophysicist should devote himself to physical measurement of the three basic phenomena of circulation: pressure, volume of flow, and velocity of flow. Instruments like the ballistocardiograph, electrokymograph, capacitance cardiometer, and electromagnetic flowmeter are physical in nature and need further study for their successful application. Already, the diagnosis and treatment of cardiovascular disease are benefiting from the application of physical instrumentation and theory to circulatory problems.

Obviously, the position of nuclear physics in biology is an important one. It includes the study of nuclear radiations for tracer isotope investigations, the effects of nuclear radiations on living matter, and a thorough treatment of the hazards involved in handling radioactive materials. The physical nature of this body of information is sufficiently clear to make further exposition superfluous. In the program currently being developed at the Ohio State University a separate course equivalent to that embracing all the other subfields of biophysics is devoted to radiation.

Another facet of biophysics is the study of the mathematical analysis of biological phenomena, which is the major thesis of the group headed by Rashevsky (1948). Unfortunately, research in this area requires more training in mathematics than most biologists have had. However, the amount of training necessary for an understanding of the material need not go much beyond the calculus; and as soon as biology students are aware of their need in this respect, the existing deficiency may be corrected.

Physical instrumentation forms a major portion of the projected activity of the biophysicist. In the past two decades electronics has assumed the dimensions of a complete science, and many measurements are now possible that previously awaited development of physical methods for transduction, amplification, and recording. The design of apparatus with correct frequency response and recordable output, with sufficient linearity for accuracy and without instrumental hysteresis or other apparatus artifact, requires intimate

knowledge of a large number of available types of equipment. To learn of the existence and application of this equipment, and to keep abreast of the prolific output of the instrument makers, will require a significant portion of the biophysicist's time. Further, the latter must learn how to pass on to the biologist the theory of coupling mechanisms, damping, conversion of energies, properties and parameters of physical systems, and other information relating to instrumentation and applicable to the analysis of life.

Collectively, the body of information in these several fields is "biophysics." There are, of course, other directions in which the categorization might proceed, and in no case is the list of material in any group complete. With this definition as a beginning, however, a working concept of the scope of biophysics can and will be evolved.

The biophysicist should know all these fields well enough to teach them to students without omitting either the physics or biology. He should be able to discern places where application of physical thought and techniques is indicated. He should know reasonably well both the physical and biological literature on each subject, and he should keep abreast of the developments in both fields. In the specific field in which he does research, he must be capable of bringing about a union of biological and physical thought. These are rigid standards, of course. However, as the training of biophysicists becomes coherent and more uniform, and the literature is collected, the maintenance of standards will become less difficult.

Biophysics as a Separate Science

It is easy to see that biophysics covers a very large quantity of information. Most of the material is included in the literature of other fields, and the effect of this intellectual obesity is reflected in the tremendous size of reference books in the biological sciences. No graduate student of biology even attempts to learn thoroughly all the information thus presented to him and, in fact, the biophysical information is often made easy to skip by being printed in small type. Exceptions to the contrary, most graduate curricula in biology simply ignore or pass over lightly the detailed study of physical phenomena.

Of equal importance is the fact that physics is also growing rapidly and has reached immense proportions. The normal three- or four-year curriculum of the graduate course in biology does not allow time for the study of physics, and the physics student has no time to devote to biological studies. For the biology student to acquire the physics necessary to apply physical thought and techniques intelligently to biology would require two or three years of additional training. No one relishes the idea of a long extension of his educational period. Therefore, irrespective of the feelings of the observer, he must conclude that the only solution to this problem is the establishment of a separate discipline for the pursuit of biophysics. The training program should be designed to provide a working knowledge of both biology and physics, and it should stress those aspects of biophysics that are peculiar to neither biology nor physics.

This idea will bring forth howls of protest from many quarters, for there are those who claim (and rightly so) that there is already too much specialization in science. There are many who think that, if one is sufficiently interested in the application of physics to biology, he will get the training he needs, even though it is not immediately available to him. There will be a few such persons, but the production of biophysicists will not be sufficient to meet the demand for them if one relies on such haphazard means. There would be no control of the quality of training of persons who enter the field in this way. To put the issue bluntly, if the opponents of specialization can produce adequate numbers of biophysicists to meet the standards we have set without resorting to specialization, let them do so. Such a demonstration would decide the matter.

People who recognize the need for specialization in this respect must work for it in the face of opposition. In five or fifty years, biophysics will become a mature, separate science, and it will flourish because it is needed. The danger of separation of biophysics from biology is that of loss of liaison between the two fields. This must not occur, for the biophysicist can function well only so long as he retains his knowledge of biological thinking and methodology. There are also hazards in the administrative details of a complete severance of biophysics from the other disciplines of biology. It is wise, therefore, to present an alternative to the unequivocal separation of biophysics from biology. One possibility is the incorporation of biophysics in departments of physiology, zoology, or botany.

In schools of medicine, where biophysics is likely to grow most rapidly, the physiology departments are the logical homes for biophysics. There is little doubt that, in the future, the field of biophysics will grow to such proportions that the creation of a separate department will be imperative, and in some institutions it may even now be desirable. For those institutions in which the position of biophysics is tenuous, however, a more or less brief period as a subdivision of a physiology department is likely to be valuable. It must be emphasized that, if biophysics does develop under the auspices of another department, the people concerned must retain the authority to ascertain the direction of their researches, to train others in biophysics, and to call themselves "biophysicists." They must have sufficient autonomy to decide on biophysics curricula and training programs. Their background must, of necessity, differ from that of other biologists, and this will make mutual understanding difficult; but I believe it is important that a person engaged in the activities of either a department of biophysics or a subdivision of biophysics in another department should have the title "Professor (or Assistant or Associate) of Biophysics," so that he may

perform his tasks without danger of confusing his duties with those of other persons. The original recipients of the title may not have the training to warrant it, but careful selection of these people for their interest in the field and their background should partially solve this problem. Eventually they will pass on and leave true biophysicists in their wake.

Sources of Biophysics Students

The training of a biophysicist will be no easy task, especially as there is now no pattern set for his training. Before instruction can even begin, there is one question which must be answered—namely, whether biophysicists should be sought among students in the biological sciences or in physics. In a symposium on biophysics held at the Johnson Foundation for Biophysics, University of Pennsylvania (1938), Detlev Bronk presented a very good case for the training of biophysicists from persons already educated in physics. A. C. Burton (1949) also feels that such individuals are better equipped for biophysical training than are biologists, and A. V. Hill is a notable advocate of this idea.

Unfortunately, physicists who work in fields other than their own do not acquire a name for themselves among their fellows, and that name is important to their advancement. Young physicists will not be interested in a field that is merely an application of the "meat" of their training, but will wish to pursue activities leading to fame and fortune in physics. Furthermore, the salary scale in physics is higher than that in the biological sciences, because of the active demand for physicists, and the discrepancy is not likely to disappear in the near future. Moreover, the physicist does not ordinarily acquire a "biological turn of mind." He is accustomed to experiments with a reasonably narrow range of variation, and he is trained in the design of experiments with few variables. To work in biophysics, he must first learn the techniques used in controlling many variables, and this involves special biological training, which takes time. The one or two or three years of training in addition to that he has already received will deter many a young scientist, who will want to begin professional activity as early as possible.

Biologists, also, usually lack the necessary background for training in biophysics. Whether we like it or not, there is a difference in the approaches that physicists and biologists take in tackling problems, and the student of biology is acquainted only with the biological way of thinking. We must recognize this difference in evaluating the advisability of training either physics or biology students in biophysics. As with the physics student, the biology student would require some years of special training, and biologists have the same objections to extra training that the physicists have.

The fact remains that biophysics involves the application of the physical way of thinking and the techniques to biology. Unless a biophysicist is trained accordingly, he will not be successful in the field. Therefore, adequate training in both physics and biology is essential, but which of the disciplines is followed first is not important. Students may be drawn from either field. The problem is not one of choice of students, but one of making students of either field sufficiently interested to pursue the extra studies and labors required to wed the disciplines. Ideally, this fusion would begin early, and special curricula should be designed for undergraduate students who propose to enter graduate work in biophysics. Naturally, demand for such students must be created before their training is practical. This is another problem in the evolution of biophysics that must await further development for a satisfactory answer, but for which temporary expedients may suffice quite well.

A Suggested Graduate Curriculum in Biophysics

The successful training of biophysicists obviously depends on the development of an acceptable curriculum for the student to follow. This curriculum must be sufficiently broad in scope to produce the desired result, but must also be practical from the standpoint of time and facilities. The discussion that follows presents only one of several possible curricula which would give proper training to biophysics students, and it is intended only as a suggestion. It has never been tested. It is designed to give the maximum education in biology and physics, in what is considered a reasonable length of time for graduate study (four years).

Ideally, the decision to become a biophysicist should be made in early undergraduate work, so that training in elementary physics and biology can be directed intelligently. If this is possible, the basic training in physics, zoology, botany, chemistry, mathematics, and anatomy can be acquired before graduate work is begun. Thus, emphasis is placed on the need for propaganda at the undergraduate level, by deans and advisers in arts and sciences colleges, and by instructors in physics and biology. At present it is not evident that an undergraduate degree in biophysics will do anyone any good, but in the future there may be a demand for workers with an orientation knowledge of biophysics. Such persons might be useful in instrument design, manufacture, and sales.

For much of the routine work in laboratories of biophysics, a level of training equivalent to the master's degree would be adequate. In the one or two years usually devoted to earning the master's degree, the student could not be expected to absorb enough biology and physics to pursue independent research on his own, but he can become thoroughly enough acquainted with biophysical techniques to apply them under direction. In the radiological defense program of the Armed Forces, students at Ohio State University do acquire a reasonable knowledge of the field. However, these students have had special preparation for the work, and they must spend some time in the Atomic Energy Commission laboratories, besides the two years they spend in didactic work and research at the uni-

versity. At the end of their training periods, they receive a joint master's degree in physics and physiology.

Unfortunately, it is rare that one becomes interested in a field like biophysics before graduate work is begun. Therefore, deficiencies in preliminary training usually exist, and the program of graduate study must first make up these deficiencies before providing the more advanced training required for qualified biophysicists.

In the graduate program of training a compromise between the desirable courses and practical time limitation is obviously in order. The first year must be at least partially used in making up existing deficiencies. By the end of this first year, the student would ideally have finished successfully courses in differential equations, statistics, engineering physics on a higher level than the usual elementary physics, physical chemistry, biochemistry, and physiology. The biochemistry and physiology should be on a level at least comparable with courses offered in the medical schools. This is a formidable list of subjects, and in some schools it may not be practical from the standpoint of course offerings. Actual curricula may vary with respect to individual courses but should not deviate appreciably in the over-all content of the first year's work.

During the second year, the student might receive course instruction in general physiology (with special emphasis on the application of physical chemistry to biology), classical biophysics, and radiation biophysics in the biological sciences; and nuclear physics, wave theory, mechanics, and any other advanced physics courses he can work in. If possible, courses in neurology and histology should be taken. The student should by this time be regularly attending seminars in physiology and special seminars in biophysics. His contact with the biophysics teaching staff will have developed to the point where work on a dissertation problem may begin.

The third year should be spent on research, for the most part, although special courses in instrumentation and electronics are desirable at this time. A regularly assigned reading program should be designed to help the student acquire supplementary information of biophysical nature, and he should become thoroughly acquainted with the literature of biophysics. Toward the end of this third year, examinations might take up the majority of the student's attention, for he will be about ready for the preliminary orals at this time. Any language requirements should have been worked off by the end of this year.

In the fourth year, the procedure would be the same as in any of the sciences, and the time would be largely devoted to finishing the dissertation and taking final examinations.

With such a program as this, the student will have obtained the course work usually required for a master's degree in biology, and about the same in physics. In addition, he will have put considerable emphasis on the problems peculiar to the field of biophysics and, if his dissertation is acceptable and his understanding of the field is adequate, he will be entitled to the degree Doctor of Philosophy in Biophysics.

It should be reemphasized at this point that this is only a suggested approach to the graduate study of biophysics, and there may be many other programs with equal or greater practicability. In any suggested curriculum such as this, there will be corrections and revisions to make and, of course, the curriculum will be modified according to the courses available to the student. The actual success of any graduate program in biophysics will depend on the men who direct the graduate work. Slipshod advising, ignorance of what is needed by the student, lack of interest in teaching biophysics, or poor organization of the program will all spell failure, and failure cannot be tolerated in a field that is not yet fully established. Therefore, before any program for graduate training is set up, the faculty should be scrutinized carefully for the necessary qualifications. If possible, the students should initially be selected with more than ordinary care, and their training should be conscientiously supervised, for these students will go on to train others and the future of the field may depend on them.

Even when graduate training of biophysicists is undertaken in physiology departments, the degree given should be in biophysics, so that the world will know the nature of the training of the individual. This will be important to his future, for selection of biophysicists will eventually be based upon training and the volume and nature of published research, and not upon unsubstantiated claims of being a biophysicist.

The Usefulness of the Biophysicist

The biophysicist will have plenty to do. In the medical professions few people (especially those who use physical equipment) are adequately trained in physics. Indeed, it is the expressed opinion of many who are in the business of designing instruments for the medical profession that it is fatal to leave a hole in the apparatus large enough for the user to stick his finger into, for, if it is there, the finger or the apparatus will suffer. Another way of stating this sentiment is that, in designing a medical instrument, one makes it foolproof, then goes further to make it nurse-proof. It is difficult to make the instrument doctor-proof, for doctors carry screwdrivers in their pockets.

If amusing, the situation is also serious, for it means that educators in the basic sciences have failed to emphasize this important facet in the training of medical students. It is not only in instrumentation that these students are lacking, for frequently a promising line of medical research will be dropped when the investigator reaches the limits of his inadequate physical knowledge. The basic ethics of medicine demand that a physician, in treating a patient, shall know when he needs a consultation and whom to consult. This precept is scrupulously followed. In planning research, however, the physician or surgeon may not realize that he needs a consultation, or he may consult the wrong person. Physicians need not be biophysicists, but they do need an introduction to biophysics suffi-

ciently extensive to tell what is possible, and to know where they need to go to learn what they do not know. The medical curriculum is already overcrowded, but sufficient time for such an important phase of training in all specialties of medicine will certainly be found when medical educators become aware of the need, and when the biophysicists are available.

Although they are not often aware of it, physicists also have a gap in their training. They set out to study in detail the physical phenomena of the world about them, but do not take into account man himself, who is the ultimate observing instrument for all physics. Physicists should receive some training in biology, and it would strike home more effectively if such training were of immediate interest in their own field.

The most important task of the biophysicist is that of teaching graduate students in biophysics. The developments in the philosophy of biophysics in the next few years will determine the type of training these students will receive, and we can rest assured that, with the large number of competent scientists now becoming interested in training biophysicists, training will move in the direction calculated to make biophysicists most valuable to society. In the teaching of graduate students in physiology, zoology, botany, and bacteriology, biophysics is assuming a more and more important role. Such students already get adequate training in chemistry, but their physics training is often neglected. In general, their only contact with physics is a single sophomore course, taken because it is required. Any physiologist will concur in the idea that his field embraces the physics and chemistry of living matter. The physical portion of such studies certainly should not be slighted.

There are thus at least four major groups who need training in biophysics. Who is to give them such training? Obviously, there must be especially trained personnel prepared to teach biophysics, perform biophysical experiments, guide the biologist and physicist in their work, and teach others, that the field may continue in its usefulness.

Dr. Burton (1949) has placed considerable emphasis on the role of the biophysicist in performing purely administrative duties, such as consultation on problems of measurement, furnishing special physical materials, administration of shop procedure, and maintenance of an electronic construction and repair service. Such duties are certainly a part of the biophysicist's job. However, extreme caution must be exercised that these service functions do not take up more than their fair share of the biophysicist's time, to the exclusion of other duties. To conceive and execute the construction of an instrument for measurement of a biological phenomenon is a worthy undertaking. Much of the work involved is purely routine manual labor, however. The wiring of circuits, the machining of parts for instruments, and their testing on completion can well be placed in the hands of competent technicians. The biophysicist will be most useful as a consultant on instrumentation problems, not as a mechanic to build the instruments. Give the biophysicist control of machine shop and electronic construction facilities, and he can turn out the required instruments and still perform many more useful and significant functions.

The duties I have listed are those performed in academic positions in biophysics. These academic jobs will be in medical schools, liberal arts schools where graduate physicists and biologists are trained, and in technological schools where engineers are given broad education. In addition, as departments and university laboratories of biophysics become better financed, there will be many research jobs associated with university activities. These jobs should be filled by competent, hence specially trained, biophysicists.

The military laboratories likewise offer excellent opportunities. I can imagine openings for such persons in laboratories like the Aero Medical Laboratory at Wright Field; The School of Aviation Medicine at Randolph Field; the Naval Research Laboratories at Pensacola, New London, Bethesda, and elsewhere; Army laboratories concerned with problems of chemical and biological warfare, soldier welfare, cold and hot weather operations, and many others. There will also be positions in purely research organizations such as the Rockefeller Institute, National Institutes of Health, and so on.

The industrial field will be a fruitful one for biophysicists in the future, especially in industries manufacturing apparatus to be used by biologists and physicians. There will be administrative jobs with organizations like the Office of Naval Research, or the National Science Foundation when it becomes activated. The laboratories concerned with atomic energy (such as those at Oak Ridge, Brookhaven, Argonne, Hanford, and Los Alamos) may use many well-trained biophysicists when they become available.

The list of potential uses for biophysicists could go on and on, of course. Those given here will strengthen one of the essential points this article desires to make, to wit: The specially trained biophysicist is sorely needed, and he probably will never starve.

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Technical Papers

The Physiologic Limits of Vision in Physiographic Observation

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Since the physiographic studies of Davis (*1*) and Keith (*2*) in the Appalachian-New England region near the end of the 19th century, geomorphologists have been divided into two schools of thought concerning the appearance and nature of upland surfaces. The concept of the followers of Davis seems to have been derived from his exhortation:

> Ascend a hill that reaches the general upland level, and note how even the skyline is on all sides; how moderate the unequality of the surface would be if it were not for the few mountains that rise above it, and the many valleys that sink below it. Looking around the horizon, the slightly rolling high-level surface of one hill after another approaches the plane of the circular skyline. It requires but little imagination to recognize in the successive hilltops the dissected remnants of a once even and continuous surface, beneath which the valleys of today have been eroded (*3*).

Keith (*4*) and his successors, in contrast, are convinced that the identical mountain areas consist of a number of planed surfaces separated by small vertical intervals.

The fact that two groups of workers see different features in the same landscapes, not only in the Appalachians and New England, but in the Rocky Mountains as well, creates a problem that merits attention, if only because the interpretation of geomorphic history depends on a correct description of the landforms involved. The adherents of both concepts have stressed the importance of field observation, but the proponents of multiple surfaces have also emphasized the necessity of checking field work with map study by means of "projected" (*5*) and "zonal" (*6*) profiles.

From the great reliance placed on what the eye sees in a landscape, it is evident that the physiologic limitations of the human eye as an observational instrument have never been considered in physiographic work. In fact, Davis dismissed the matter summarily: "Considerable as the inequalities of altitude are, frequent study of the maps and repeated views of the uplands from various hill-tops impress me more with the relative accordance of the altitudes than with their diversity. I cannot admit that the appearance of accordance from hill-top to hill-top is an optical deception" (*7*).

It is not the purpose of the authors to discuss the amount of relief that is admissible in "an even and continuous surface," or the external factors that impose limitations on observation, such as atmospheric phenomena and the curvature of the earth. The latter subject has been covered adequately from every angle in numerous papers and needs little comment. Nevertheless, one factor in connection with Davis' quotation should be noted. Unless there is a broad depression between the observer on a hilltop and the upland surface that he is examining, he is not looking at the same surface as that on which he is standing, but at a higher level because of the curvature of the earth.

The present study will consider factors within the eye itself that impose limitations on physiographic observation. Because of the structure of the retina, there is a definite limit to the magnitude of relief that the human eye can perceive at a given distance. The perceptive mechanism of the retina is a closely spaced array of photosensitive nerve endings, the cones. The physical limit of definition depends on the spacing of the cones. To discriminate the form of an object, its several parts must be differentiated, and this necessitates the stimulation of separate cones. Microscopic measurements (*8*) have determined the average diameter of the macular cone as .004 mm, thus establishing the smallest distance between 2 cones. The normal eye should be able to perceive form in an image made up of component elements spaced .004 mm apart.

TABLE 1

THE SNELLEN TEST TYPES (*10*)

Line on chart	Distance						Size of letters	
1	Standardized	to	60	m,	or	196.85 ft	87.0	mm
2	"	"	36	"	"	118.11 "	52.2	"
3	"	"	24	"	"	78.74 "	34.8	"
4	"	"	18	"	"	59.05 "	26.1	"
5	"	"	12	"	"	39.37 "	17.4	"
6	"	"	9	"	"	29.53 "	13.05	"
7	"	"	6	"	"	19.68 "	8.7	"
8	"	"	4.5	"	"	14.76 "	6.53	"
9	"	"	3	"	"	9.84 "	4.35	"

The eye comprises a simple lens and screen system; hence it follows that image size is determined by the eye's distance from the object. It has been found that, in order to produce a minimal image, an object must subtend a visual angle of 1′ with the retina (*9*). This is the standard of normal visual acuity. The Snellen Test Types are constructed on these principles and are accepted standards for determining visual acuity. The types consist of rows of letters that diminish in size, scaled so that at specific distances, each letter subtends a 5′ angle and each component part of a letter a 1′ angle with the retina (Table 1). Visual acuity is recorded as a fraction, the numerator denoting the distance between the type and the patient, and the denominator, the test line that he reads. The normal eye should distinguish the letters in the 6-m,

FIG. 1.

or 20 ft, line at a distance of 6 m, or 20 ft. If such is the case, it is recorded as 6/6 or 20/20. The statement "20-20" vision refers to this fraction. The chart is best illuminated by 80–100 ft-c.

By adopting the principles used in developing the Snellen Test Types, but using larger objects and greater distances, it is possible to determine the point at which individual features in a landscape cease to be differentiated. It is assumed that the illumination of the object observed is of the same order of magnitude as that used for the Snellen Type Tests for visual acuity. Furthermore, the geomorphologist is postulated to have 20/20 vision. For example, a cliff 100 ft high, at a distance of 13.06 miles, will subtend an angle of 5′, as does the letter of the Snellen "20-20" line viewed at its standard distance of 20 ft. It will be just perceived as a discontinuity of form by a person with "normal" vision. This statement must be understood as semiqualitative, as illustrated by Fig. 1 when viewed by the reader at a distance of 20 ft. In this illustration, the Snellen letter is a sharply defined black figure on a white background (*11*), which offers maximum contrast. The horizon line of the profile, on the contrary, consists of an undulating form, so that only abrupt declivities are equally conspicuous. In actuality, the sky and landscape offer a black-and-white contrast only under most unusual conditions of atmospheric clarity and lighting. When reduced illumination, haze, or subtility of contour obtains, greater changes in relief are necessary for perception.

The preceding discussion leads to a simple rule for field observation: a 100-ft cliff at 13 miles will be just perceptible under optimum conditions. At one-half the distance, a 50-ft cliff will subtend the same angle and offer similar geometric contrast. Under poor illumination, a precipice several times this scale would be necessary for discernment. With the dispersion of light caused by haze, a further allowance should be made, particularly for distant skylines. Therefore, although a horizontal surface separated from another such bench by a 100-ft cliff could be seen by a physiographer with "normal" visual acuity under ideal atmospheric conditions, it might easily be overlooked. The two surfaces, in this case, would be described erroneously as a single-planed surface of low relief. From consideration of the physical and concomitant external factors that may produce optical deception, it is apparent that descriptions of topographic relief based on the eye alone are not reliable.

The physiologic limitation of the human eye is offered as a plausible reason for different physiographic descriptions of identical upland areas. Lack of consideration and evaluation of this factor may explain why some geomorphologists have seen but one "even and continuous surface" in uplands, whereas others have identified a number of beveled surfaces separated by small vertical intervals. The former dismiss as minor (or perhaps do not see) the minute details noted by the latter.

It thus appears that "the optical deception" of hilltop accordance that Davis would not admit may very well be a fact. Like his colleagues in other fields of science, the physiographer finds that his eyes have a finite limit of reliability, and he is therefore driven to search for other methods of checking observations of topographic forms than by eye alone—namely, map analysis. Although he may be deprived of the comfort that what he sees is real, nevertheless, the foregoing simple formula may be of some assistance in determining the approximate height of features, where distances are known, by providing a scale of relief in which 100 vertical ft at 13 miles' distance will be barely perceptible under ideal conditions.

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Intracellular Localization and Distribution of Carbonic Anhydrase in Plants[1]

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Steemann Neilson and Kristiansen (*1*) have recently reported that in the aquatic plants *Fontinalis dalecarlica* L. and *Elodea canadensis* Mich. carbonic anhydrase is limited to the chloroplast sediment obtained by centrifuging the filtered leaf brei. This observation agrees with that of Day and Franklin (*2*), who found that carbonic anhydrase is confined to the chloroplast sediment obtained from leaves of *Sambucus canadensis* L. As Steemann Neilson and Krist-

[1] This investigation was conducted in the Plant Science Laboratories of the Division of Applied Biology, National Research Council of Canada, Ottawa. Issued as N. R. C. No. 2318.

iansen pointed out (*1*), these results indicate that the enzyme is located in or on the chloroplasts, contrary to those of Bradfield (*3*), who found the enzyme only in the leaf cytoplasm of herbaceous land plants. Neish (*4*), who provided the first evidence of carbonic anhydrase in green leaves, found the enzyme distributed between the chloroplast and cytoplasm fractions.

Using a manometric technique, modified after the boat method (*5*), we have reinvestigated the distribution and intracellular localization of carbonic anhydrase in land and aquatic plants. Our enzyme unit E.u. is the ratio $\frac{R-Ro}{Ro}$ (*5*), determined at 10° C by adding 0.5 ml 0.2*M* $NaHCO_3$ in 0.02*M* NaOH to 1.0 ml 0.2*M* phosphate buffer (pH 6.8), with and without enzyme solution. Leaf extracts were prepared by grinding and expressing the juice through nylon. The chloroplasts were sedimented by centrifuging at low temperature for 15 min at 15,000 *g*. The carbonic anhydrase activities of the uncentrifuged extract, supernatant, and resuspended chloroplast fractions were determined, using an enzyme-limited system. The enzyme was found in the leaves of 21 of the 23 species tested. Cysteine (0.01*M*) had little effect on the observed enzyme activity. The activity observed in the leaves of land plants varied from 5–20 E.u./ml leaf extract in monocotyledons (*Triticum vulgare* Vill., *Panicum miliaceum* L., *Hordeum vulgare* L. and *Tradescantia fluminensis* Vell.) to 120–160 E.u./ml in the most active dicotyledons (*Tetragonia expansa* Thunb., *Spinacea oleracea* L., *Tropaeolum majus* L., and *S. canadensis* L.). The major part of the carbonic anhydrase was found in the supernatant fraction of most of the examined species, including *S. canadensis* L. The aquatic plants and *S. racemosa* L. were exceptional in that the enzyme was apparently limited to their chloroplast sediments. Concentrated chloroplast suspensions prepared from the aquatic plants (*Potamogeton* spp., *Myriophyllum* spp., and *Elodea canadensis* L.), however, showed very low activities in either the presence or absence of 0.01*M* cysteine (*3*). Enzyme activity could be detected when the chloroplasts were suspended in 1/12 of the original volume, as compared to the thirtyfold concentration employed by Steemann Nielson and Kristiansen (*1*). The activity was reduced below the limits of measurement when chloroplasts from the aquatic species were suspended in the original volume of liquid, and usually could not be detected in the uncentrifuged leaf extracts. It seems unwise to draw conclusions as to the intracellular localization of carbonic anhydrase on the basis of observations on aquatic leaves (*1*) which contain less than 1% of the activity found in the leaves of land plants. The fact remains, however, that aquatic species such as *E. canadensis*, which can use HCO_3^- from the surrounding medium for photosynthesis, do contain detectable amounts of carbonic anhydrase, as reported by Steemann Nielson and Kristiansen (*1*).

The apparent restriction of carbonic anhydrase to the chloroplasts of the land plant *S. racemosa* L., which had previously been reported for *S. canadensis* L. by Day and Franklin (*2*), was found to be an artifact. A natural flocculating agent in the cell sap, believed to be tannin, causes the cytoplasmic proteins and chloroplasts to be deposited together when centrifuged. Negligible protein remains in the supernatant liquid after centrifuging. On resuspending the crude chloroplast sediment in water and adjusting the pH upward from 6.1 to 8–10, it was observed that the cytoplasmic proteins, including carbonic anhydrase, were dispersed, and that the major part of the activity remained in the supernatant fraction after centrifugation. Similarly, when *S. racemosa* leaves were crushed in dilute alkali, flocculation of the cytoplasmic proteins was prevented, and the greater part of the carbonic anhydrase remained in solution when the chloroplasts were removed by centrifuging. In other land plants a minor part of the enzyme activity was often recovered in the chloroplast sediment. This residual activity, however, was almost entirely removed by washing the chloroplasts with water. It is therefore concluded that the carbonic anhydrase of land plants is localized in the leaf cytoplasm and that this may be equally true of the aquatics.

Interest in plant carbonic anhydrase stems from the role it may play in photosynthesis. If carbon dioxide is used as HCO_3^- ions in photosynthesis, carbonic anhydrase would be required to catalyze carbon dioxide hydration at the rate of photosynthesis in strong light (*6*). Our observations include several indicating that carbonic anhydrase is connected with photosynthesis and that it is an adaptive enzyme. Bradfield (*3*) has already reported that plants showing high carbonic anhydrase activity in their leaves do not show detectable activity in their roots. We have observed that the white parts of variegated *Tradescantia* leaves contain 50% less carbonic anhydrase per ml extract than the green parts. Albino barley leaves contain 75% less carbonic anhydrase than normal barley leaves of the same size and age. On excluding light from *Tropaeolum majus* and *Petroselinum hortense* plants for 4 days, the carbonic anhydrase activity of the slightly chlorotic leaves was 55% and 30% less than that of the controls. Very young leaves of *Tetragonia expansa* are lower in carbonic anhydrase than mature leaves, expressed as E.u. per ml extract or per g fresh weight. The capacity for photosynthesis and Hill reactions is known to undergo a similar increase in the early stages of leaf development (*7, 8*).

The cyanide-sensitive reaction(s) of photosynthesis are believed to be connected with the cytoplasmic fixation of carbon dioxide rather than with the photochemical production of reducing power by the chloroplasts. (The Hill reactions of isolated chloroplasts are not inhibited [*9*], whereas the dark fixation of CO_2 by living cells can be abolished by cyanide [*10*].) We have observed 50% inhibition of plant car-

bonic anhydrase in crude extracts, and 75% inhibition in dialyzed extracts by 10^{-3} *M* KCN. We believe that plant carbonic anhydrase contributes to, but is not entirely responsible for, the cyanide-sensitivity of photosynthesis in land plants. A detailed presentation of these and related investigations of carbonic anhydrase in plants appeared in Section C, *Canadian Journal of Research.* (C **28**, 673 [1950]).

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Animal Protein Factor for the Rat Present in Crude Casein and its Relationships with Vitamin B_{12}[1,2]

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The existence of unknown factors essential to the nutrition of many organisms and present in small amounts in animal protein, and consequently generally denominated animal protein factors (A.P.F.), has been substantiated by several researches, mainly in the field of poultry science. Cary and Hartman *et al.* in 1946 (*1*) reported that an unidentified factor, soluble in hot alcohol (*X* factor), and found in crude casein and liver extracts, is required by the rat for growth, reproduction, and lactation. Further studies (*2*) presented evidence that factor *X* is present even in certain leafy foods. Shortly thereafter, Zucker and coworkers (*3*) reported that a new factor, present in animal protein, and absent from vegetables, soluble in water, dilute acid, alkali, and alcohol-insoluble, is indispensable for rats. This factor was named "zoopherin." Zucker and Zucker (*3*), feeding rats on a complete, purified diet, devoid of zoopherin, observed a high mortality in the newborn, resulting from hemorrhagic lesions in the upper part of the stomach.

For two years we have investigated the effects on rats of a factor present in crude casein. The observations collected, the lesions noted, the kind of diet used, and relationship of the factor to vitamin B_{12} lead us to publish the results.

[1] We wish to thank Cesare Barbieri, of the American Committee, University of Bologna, New York, for having supplied us with the vitamin B_{12}, a product of the American Roland Corporation, used in this investigation.

[2] We acknowledge the assistance of M. A. Dina, of the Pathological Anatomy Institute of the University of Bologna, in the histological examinations of the lesions described.

Rats of our strain were fed the Randoin and Causeret (*4*) diet, which is not a synthetic diet, but rather a natural and extremely varied nourishment. This diet consists of:

	Percentage
Ground cereals (wheat, maize, barley, oats, rye)	88
Wheat germ	5
Crude casein	5
Wheat germ	1.5
Crude casein	0.5

Twice a week the animals also received carrots and vegetables *ad lib.* (salad, lettuce, cabbage, cress, broccoli) and dry yeast. With such a diet Randoin (*4*) and one of us (*5*) have observed optimal growth, reproduction, and lactation for several generations.

Crude casein was the only source of animal protein in this diet. Experiments were then carried out replacing crude with purified casein, made as follows. Casein was suspended in water containing 0.5% acetic acid and a few drops of chloroform. The ingredients were thoroughly mixed, and after slow decantation the liquid was discarded and replaced with new water. The procedure was repeated three times a day for 2 weeks. Finally, the casein was centrifuged down and desiccated *in vacuo*. The animals were kept in special cages in order to avoid possible coprophagy.

A first group of 25 female rats fed a Randoin diet containing purified casein exhibited normal growth, as well as regular reproduction and lactation. The young born of such females (1st generation) exhibited high mortality: 89 out of 126 young rats died (70.6%). The surviving rats reached an almost normal growth: 7 females were able to reproduce. Absolute mortality (100%) was shown by the young of these females (2nd generation). Death did not occur during the first few days of life, but usually between

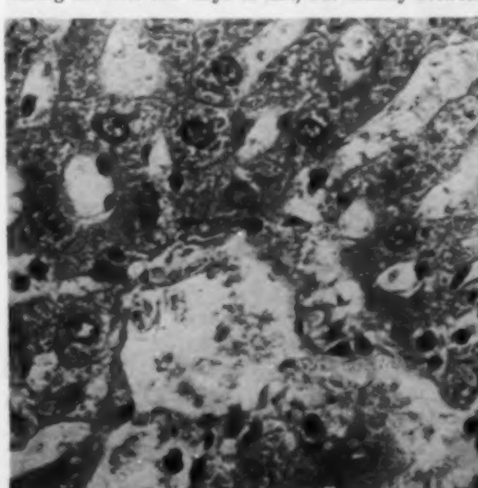

FIG. 1. Normal liver (×720).

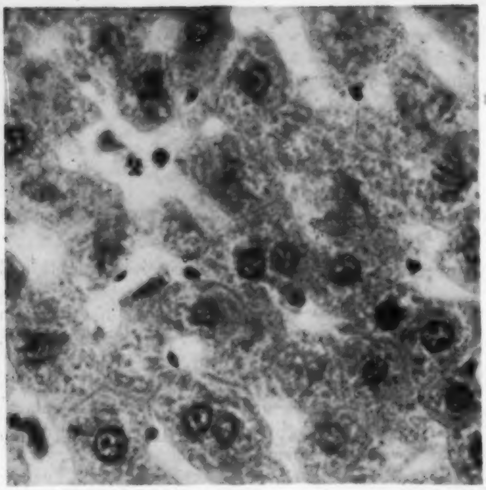

FIG. 2. Liver of rat fed a diet containing purified casein (×720). Hepatic cells show protoplasmic swelling with granular aspect. Nuclear polymorphism showing some karyorexis. Increase of binuclear cells; increase of Kupffer cells, and limphomonocytic proliferation.

the 15th and 20th days and only rarely after weaning. It is emphasized that the reproductive ability of these females is generally below normal. In addition, the average weight of the newborn of females on a deficient diet is always below normal (av, 3 g instead of 4.4).

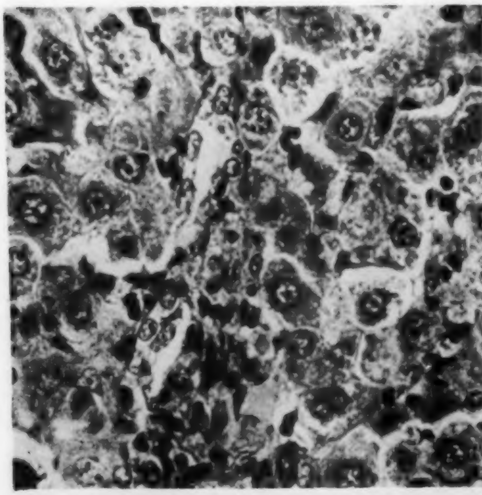

FIG. 3. Liver of rat of the 1st generation (×720). Diffused protoplasmic swelling of granular and microvacuolar type, with lysis of the hepatic cells and necrobiosis of some isolated elements. Notable nuclear polymorphism, with karyorexis, karyolysis, and chromatin dispersion in the cell. Frequent regenerative phenomena with binuclear cells; irregular hyperchromic nuclei. Enlargement of Kupffer cells, with an intense lymphomonocytary proliferation having the aspect of interstitial hepatitis.

The principal and most serious lesions exhibited by the animals of the 1st and 2nd generations, which probably caused death, were found in the liver, which always showed a very pale color.

Histological preparations of the liver of rats fed a diet containing purified casein (Fig. 2), as well as of the newborn of the 1st (Fig. 3) and 2nd (Fig. 4) generations, are shown in comparison to normal (Fig. 1).

The relationships found by Ott, Rickes, and Wood (*6*) between the animal protein factor of the chick and vitamin B_{12} led us to test the effects of vitamin B_{12} on the newborn of the 2nd generation, in which the hepatic lesions were more evident. Vitamin B_{12}, administered directly in doses of 0.5–5 μg daily,

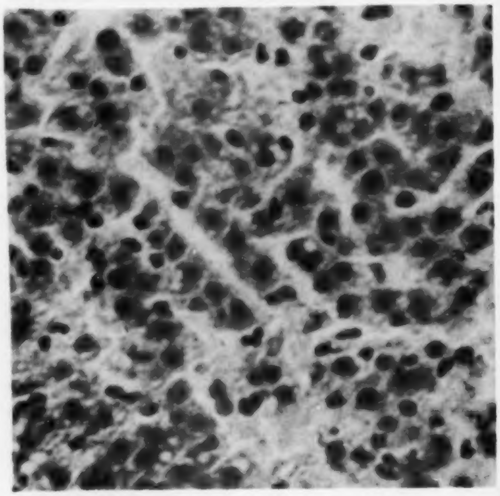

FIG. 4. Liver of newborn of the 2nd generation (×440). Strong generalized vacuolization of the hepatic cells, with necrotic and lytic zones; absence of mesenchymal reaction; noticeable nuclear polymorphism.

proved to be completely ineffective, whereas small quantities of whole cow's milk saved the animals.

Crude casein contains, therefore, a factor (or factors) indispensable for the normal growth and reproduction of rats. This factor is water-soluble, heat-stable, and scarcely oxidizable, since the crude casein was dried at 100° C in the presence of air. This factor does not seem to be identifiable with vitamin B_{12}. The factor is stored in the organism, and can be exhausted in 2 generations. A deficiency of it causes a high mortality, 70% in the 1st generation and 100% in the 2nd generation.

Death always occurs for whole litters and in a very short time, following an all-or-none principle. The particular histological aspects, and the composition of the diet used, lead us to conclude that the liver lesions described are not related to choline deficiency. In addition we have never observed the gastric hemorrhagic lesions observed previously by others (*3*).

According to our observations, we assume that more than one factor essential for the rat is present in animal proteins.

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A Micro Ball Mill for the Disintegration of Bacteria

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For grinding small quantities of bacteria a centrifuge tube with a ground-in glass rod can be quite satisfactory, but it is difficult to obtain the same mechanical effects if a number of specimens must be treated simultaneously. For this reason the vibrator equipment described below was designed.

The use of 50 cps vibrations for disintegrating biological materials has been described by E. Hammarsten (*1*). The present author found the method very useful and devised an extension of the technique, which may also prove of value for grinding other biological materials besides bacteria.

The grinding was effected in glass tubes made out of ordinary pyrex glass tubing (diam, 7 mm), which was cut about 15 cm long. The pieces were bent in the middle to resemble the tube in Fig. 1. A special holder made out of brass and containing Woods metal (Fig. 2) was heated to melt the alloy (mp 65.5° C), and the tubes were then inserted in a row. When the metal had solidified, the tubes were taken out of their setting and the material in question—mostly in the form of a freeze-dried powder—was added. Up to 42 specimens could be accommodated. Nine carefully chosen glass beads of a diameter slightly smaller than that of the tube were also added to each specimen, and the tubes were plugged with rubber stoppers. They were replaced in their settings, and a brass pole covered with a piece of rubber hose was placed in the angle of the tubes and screwed tightly down so as to keep them firmly in place. The holder was mounted on the stage of a 50 cps a.c. vibrator (Type EMR6, 70 w, 200 v, Vibroverken Ltd., Stockholm) in a freezing box at $-15°$ C. The vibrations were mainly vertical and caused the glass beads to be thrown between the walls of the tube, but owing to the slope of the branches they also developed a rotating movement (arrows, Fig. 1), which counteracted the tendency of the material to accumulate at the bottom of the tube and effected a continuous mixing of the material. Treatment for 4

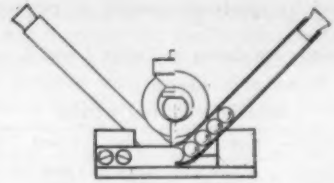

FIG. 1.

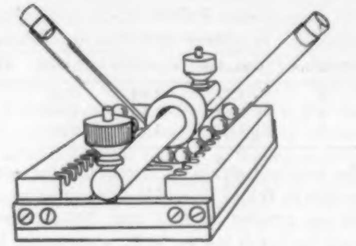

FIG. 2.

hr was not accompanied by any perceptible rise in temperature and was as a rule sufficient to break up the bacteria. The treatment could be shortened by adding weighted amounts of glass powder to the specimens or by etching the glass beads and the inside of the tubes with fluorine.

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The Purine and Pyrimidine Content of Three Strains of *Escherichia coli*[1]

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Witkin isolated a spontaneous mutant, B/r, of *E. coli* strain B which proved to be more resistant than the parent to both x-rays and ultraviolet light (*1*). These two strains, together with strain K_{12} which was found by Lederberger to show genetic recombination unusual in *E. coli* (*2*), have been analyzed for purine and pyrimidine content.

The organisms were grown in a synthetic medium, with ammonium chloride as source of nitrogen and with succinate and glutamate as source of carbon. In each case 24-hr cultures were harvested by centrifugation, and the organisms extracted with cold 7% trichloracetic acid, ethanol, and boiling ethanol-ether. The residue after being dried *in vacuo* was rendered to a powder. Approximately 10 mg of the powder was digested with $HClO_4$, the digest subjected to chromatography, and the yield of nitrogenous bases

[1] Supported by a grant from the Research Grants Division of the USPHS.

determined by spectrophotometry as previously described (3).

The results are shown in Tables 1 and 2.

TABLE 1

MICROMOLS/MG DRY WEIGHT

	Adenine	Guanine	Cytosine	Uracil	Thymine
B	.118	.150	.119	.068	.026
B/r	.127	.212	.147	.058	.026
K_{12}	.097	.158	.117	.044	.023

TABLE 2

MOLAR RATIOS

	Adenine	Guanine	Cytosine	Uracil	Thymine
B	1	1.27	1.01	0.58	0.22
B/r	1	1.67	1.16	0.46	0.20
K_{12}	1	1.63	1.21	0.45	0.24

In the resistant strain B/r, the adenine content is greater than in B by 7%, and the guanine and cytosine contents are greater by 41% and 23%, respectively. The uracil in B/r is low by 15%, whereas the thymine content is the same as in B. Thus there is approximately 56% more base in B/r than in B. Since there is no difference in thymine content, it may be assumed that this represents an increase only in pentosenucleic acid.

The survival curves for strain B with both x-rays and ultraviolet are peculiar in showing a sharp inflection at the 1% survival level (1). The curve for B/r in ultraviolet also seems to be a composite curve, with a change in slope at approximately 30%. From these curves it appears that 1% of the B population and 30% of the B/r population have the same sensitivity to ultraviolet, and the remaining 99% of B is 16 times as sensitive as the other 60% of the B/r. The difference in response to x-rays is less marked, B being not more than 3 times as sensitive as B/r.

The marked increase in guanine as compared with the other bases may be taken as evidence that the nucleic acid increase is due to cytoplasmic PNA (4) which would act as an absorbing screen around the radiation-sensitive portion of the cell, i.e., the nucleus, and thus account for the greater sensitivity of B as compared with B/r to ultraviolet light; but it seems unlikely that the additional PNA alone could account for the greater resistance of B/r to x-rays. However, since nucleic acids are capable of binding considerable amounts of metal (7), and since most of the ionization reaching the bacterial nucleus is produced by β-particles originating in the medium outside the bacterial cell, it is possible that the nucleic acid-metal complex may act as a β-particle filter and thus reduce the ionization actually reaching the nucleus. Alternatively, it may be assumed that the bacterial cell, like cells of higher organisms, has one phase in its life cycle that is more sensitive to radiation, this phase being analogous to one of the mitotic stages. Also by analogy with higher organisms, production of PNA proceeds primarily during the "resting stage," which is relatively insensitive to radiation. A mutation that would result in a decrease in the relative duration of the sensitive phase of the cell cycle would thus also be expected to produce an increase in the average PNA content of the bacteria. By this hypothesis the results with both ultraviolet and x-rays can be accounted for. Although Witkin has considered the change in shape of the survival curve in ultraviolet in B/r as compared with B as evidence against the "target theory," it seems clear from the above considerations that the apparent change in shape may have no bearing upon the target theory.

The molar ratios of the various bases are shown in Table 2.

Although strain K_{12} has an absolute base content similar to that of B (Table 1), the proportions of its various bases resemble those of B/r rather closely. In other words, K_{12} contains approximately the same amount of nucleic acid as B per unit dry weight of cells, but the composition of its nucleic acids and the relative proportions of each of these nucleic acids are similar to those of B/r.

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A Simplified Technique for Microelectrocoagulation

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During the course of an investigation dealing with the production of cardiovascular anomalies in chick embryos, we have developed and used successfully a technique for the destruction of minute areas of tissue. The method should be applicable to a wide range of investigations, particularly in the field of developmental research. Hilleman (1) used a similar technique, to obtain even smaller areas of coagulation than those required by our experiments, in destroying anlagen of pituitary glands of chick embryos. Most biological laboratories have on hand materials from which the apparatus can be assembled.

The materials needed are a dissecting microscope, a micromanipulator, microelectrodes, and a source of coagulating current. A suitable micromanipulator can be assembled quite readily by mounting an ordinary detachable-type mechanical stage on top of the rack of a compound microscope (Fig. 2. *B*). This manipulator is described in a separate publication (2).

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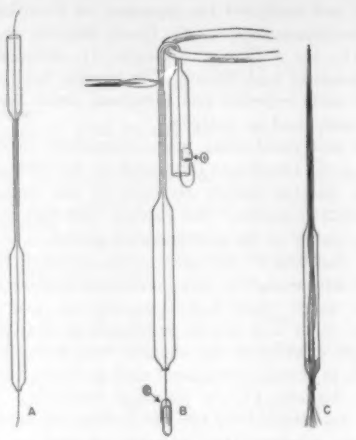

FIG. 1.

The current used is a high-frequency spark-gap current of the diathermy type, supplied by a portable electrocoagulating machine, the Hyfrecator (Fig. 2, *A*).[3] The machine emits a damped current of approxi-

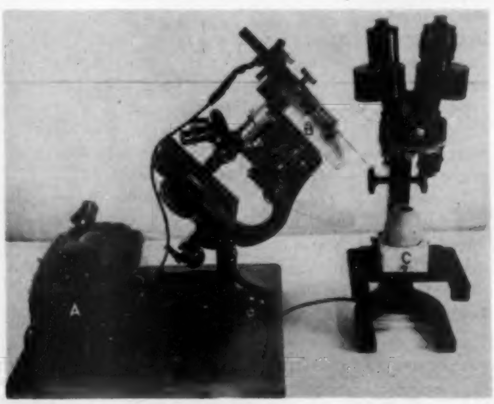

FIG. 2.

mately 1,000 kc. For our work the control knob is set at position 17, which gives an output of about 1,600 ma.

A microelectrode is made with No. 50 gauge platinum wire, which has a diameter of about 25 μ.[4] The procedure we use is as follows (see Fig. 1): A piece of ordinary glass tubing about 10 cm in length and 1 cm in diameter is drawn out over a Bunsen burner at its center to form a capillary tube approximately 15 cm in length and 1–2 mm in diameter (Fig. 1, *A*). A piece of platinum wire about 35 cm long is passed through the tubing either by threading it on a fine needle and dropping the needle through by gravity, or by threading a heavier wire through and then pulling the platinum wire through. One end of the capillary tube is heated over an alcohol lamp and bent in a U shape so that it can be suspended from a ring stand (Fig. 1, *B*). The upper end of the platinum wire is fastened to the tubing with a small piece of cellophane tape (Fig. 1, 1) and the wire is held taut by fastening to its lower end a small weight such as a paper clip (Fig. 1, 2). With a microburner the capillary tubing is heated very gently at one point until the lower part falls of its own weight, drawing out the glass to a thin film over the wire. It is then checked under a microscope to determine how far the wire extends into the fine tubing, after which it can be cut at any desired length. The tip is flamed slightly in an alcohol burner to form a small glass bead, which will seal the glass and leave about 1 mm of the wire exposed (Fig. 1, *C*). The amount of wire extending beyond the tip will depend, of course, upon the desired depth of penetration of the tissue and whether the glass tip or only the exposed wire is to penetrate the tissue. With this "hanging" method an electrode tip can be obtained in which the wire is covered by a layer of glass as thin as 10 μ. Strands of thin copper wire (obtained by untwisting a short length of common household electrical cord) are then threaded into the open end of the tubing until they impinge in the capillary tubing, making contact with the platinum wire against the side of the tubing (Fig. 1, *C*). These strands are held in place by heating sufficiently at one point to melt the glass around the wires, and by sealing them at the open end with paraffin.

The apparatus is assembled (Fig. 2) by placing the micromanipulator in position beside a dissecting microscope and fastening the electrode to the movable carriage of the mechanical stage with cellophane tape. The microelectrode is connected to one pole of the Hyfrecator as the active electrode, and a piece of metal foil applied to the bottom of the egg serves as the indifferent electrode. The latter contact is made by passing the wire from the other pole of the Hyfrecator through a hole near the base of the molded paraffin egg-holder (Fig. 2, *C*) and leaving the free end of the wire exposed. The metal foil (from chewing gum wrapper) is covered on each side with a thin layer of wet gauze and then placed in the bottom of the egg-holder. This will give a wide area of contact between the free end of the wire and the lower surface of the egg. The current from this indifferent electrode is concentrated at the tip of the active electrode, and a pinpoint area of coagulation is obtained. In general, the shorter the length of wire exposed at the tip of the electrode the more restricted will be the area of coagulation, as there may be some coagulation along the shaft of the wire. The Hyfrecator also supplies a single-pole current, with which the indifferent electrode is not necessary. With the latter type of current a conical area of coagulation is obtained with its apex

[3] The Hyfrecator is obtainable from most surgical supply dealers or can be purchased from the Birtcher Corporation, 5087 Huntington Drive, Los Angeles 32, Calif. Its cost is about $50.

[4] This wire can be obtained from The J. Bishop & Company, Platinum Works, Malvern, Pa.

at the tip of the wire and its base at the surface of the tissue; thus this can be used for superficial or surface coagulation.

In use, the tip of the electrode is placed at the desired point within the embryo, and as the foot switch is intermittently depressed the control dial is gradually advanced until the desired coagulation results. For chick embryos we used a dial setting of about 17 to obtain an area of coagulation about 40 μ in diameter, which was what we needed to interfere with the formation of the sixth aortic arch.

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Glycogen Storage in the Heart in Experimental Renal Hypertension in the Rat

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Because of the rapidity with which glycogen disappears from the heart after death, there are no data on the normal glycogen content of the human heart and, therefore, none on the effect of clinical hypertension on cardiac glycogen stores. One report (*1*) on the total carbohydrate (including lactate acid) content of human hearts obtained many hours after death from various causes is suggestive. Increase in total carbohydrate was found in the hearts of subjects that had died of cardiac diseases. We have seen no report on the effect of experimental hypertension on the storage of glycogen in the heart, though a recent report by Olsen (*2*) describes certain other chemical changes in the heart in this condition.

Nine adult rats of the piebald Evans-McCollum strain made chronically hypertensive by Grollman's (*3*)[1] method constituted the experimental group. Systolic blood pressures as measured by the tail plethysmographic method ranged between 160 and 200 mm of mercury. The animals were fasted for 24 hr and sacrificed under sodium pentobarbital anesthesia. Samples of heart, liver, and skeletal muscle were obtained and analyzed for glycogen as described in an earlier communication (*4*). Blood ketones were determined by the method of Heilesen (*5*), modified for use of a tungstic acid filtrate. Ten normal rats subjected to the same regimen and sacrificed under like conditions were used as controls.

[1] I wish to thank Arthur Grollman for supplying the hypertensive animals for these observations.

The analytical data are summarized in Table 1. There is no significant difference in the liver glycogen or the skeletal muscle glycogen in the experimental and control groups. The cardiac glycogen is significantly higher in the experimental group.

TABLE 1

TISSUE GLYCOGEN AND BLOOD KETONE LEVELS IN HYPERTENSIVE AND NORMAL RATS FASTED FOR 24 HR

Series	No. animals	Glycogen as glucose (mg/100 g tissue)			Blood ketones (mg/100 ml as hydroxybutyric acid)
		Liver	Heart	Muscle	
Normal	10	303 ± 180*	576 ± 37*	318 ± 36*	19.1 ± 6*
Hypertensive	9	363 ± 129*	761 ± 21*	410 ± 57*	15.3 ± 3*

* Standard error of mean.

The function of glycogen in the myocardium is not known with certainty. Its concentration does not vary widely under physiological conditions, and changes that do occur may not be paralleled by changes in the glycogen content of the skeletal muscles or the liver. Indeed, in certain conditions such as fasting (*6*), pancreatic diabetes (*4, 7*), phlorizin poisoning (*8*), and use of ketogenic diets (*6*) the cardiac glycogen stores increase, whereas the glycogen content of skeletal muscle and liver may decrease or remain unchanged. Evans (*9*) showed that in rats caused to swim to exhaustion there is no decrease in cardiac glycogen, though the glycogen of the gastrocnemii is markedly depleted. Shelley, Code, and Visscher (*10*) found that rats subjected to daily bouts of exhaustive exercise show increased cardiac glycogen, with myocardial hypertrophy. Exposure to low oxygen tension results in greater depletion of cardiac glycogen than of skeletal muscle glycogen, and the suggestion has been repeatedly made that cardiac glycogen is a reserve to be called upon in hypoxemic states. Glycolosis is believed to be the principal if not the sole source of energy in the anaerobically beating heart (*11*).

Lackey (*4, 6, 12*) and co-workers have shown that in a variety of conditions in which a ketonemia is produced there is a positive correlation between blood ketone levels and cardiac glycogen storage. In the present experimental series, no increase in blood ketones was found and, therefore, no evidence that the increased storage of glycogen by the heart was related to a generalized disturbance in carbohydrate utilization. It is not clear whether an increased storage of cardiac glycogen should be regarded as a reserve against emergencies or as an indication of a lessened capacity for its utilization. However, in a number of conditions in which there is an increase in the cardiac glycogen storage, the disappearance of glycogen from the heart after death is as rapid as in the hearts obtained from normal animals (*13*).

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The Direction of Flow in the Blood Vessels of the Infundibular Stalk

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Recent work, especially that of G. W. Harris (*1*), has drawn attention to a possible neurohumoral relay between the hypothalamus and the anterior lobe of the hypophysis. The neural link in the chain consists of nerve fibers from the hypothalamus to the median eminence and infundibular stem, where the humoral substance originates and is transmitted to the adenohypophysis via the hypophyseal-portal blood vessels.

The direction of blood flow in the vessels of the stalk forms an important part of the theory. Wislocki (*2*), as well as Green and Harris (*3*), suggested that the direction of flow was from the median eminence and infundibular stem to the adenohypophysis. This is in contradistinction to the report of Popa and Fielding (*4*), in the original description of the hypophyseal-portal vessels, stating the blood flow was from the anterior hypophysis up the stalk to the hypothalamus.

During recent investigations into the anatomy and physiology of the pituitary gland and stalk (*5*), a surgical procedure was developed to expose completely the stalk and rostral portion of the pituitary gland to direct vision. The operative approach was parapharyngeal, and the blood vessels supplying the hypophysis were not disturbed. It occurred to us that with this exposure the direction of flow in the blood vessels of the infundibular stalk could be visualized.

The procedures were carried out on adult albino rats. The region of the infundibular stalk was exposed surgically with the animals under ether anesthesia. By this means the blood vessels of the infundibular stalk were brought into view. The chest was then opened, and a fine glass cannula was introduced into he proximal aorta through the wall of the left ventricle. Less than 5 ml of a 50% aqueous suspension of Higgins waterproof India ink was injected slowly while the infundibular stem blood vessels were viewed with a binocular dissecting microscope. India ink usually appeared in several vessels within a few seconds of the beginning of injection. This occurred before any other vessels or tissues in the operative field became injected. With a just appreciable lag, involving perhaps no more than a second, additional vessels, usually 3 in number, became filled. By varying the quantity of ink injected, as well as the injection pressure, it was possible to fill selectively the first-mentioned vascular channels, or to fill all of them (an average of 6). It was noted repeatedly that the flow of India ink in all these vessels was invariably from the stalk to the body of the hypophysis. The vessels extended from the anterior part of the stalk posteriorly to the pituitary gland, where they ramified. They had the approximate width of a very fine silk thread. One or two of these vessels entered the posterior lobe. The pars distalis did not become colored until the India ink passed down the vessels of the stalk to the gland, nor did the distalis become colored if the stalk was severed just prior to injection. We have therefore been able to substantiate the anatomical observations of Wislocki (*2*) and Green and Harris (*3*) by direct visualization of the flow of India ink in the infundibular stalk vessels.

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A Universal Line Graph for Estimating Percentage Potency in Multidose Assays

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In 1947 the author (*1*) presented in these columns simple formulas for calculating percentage potency in 3- and 4-dose assay procedures, when the log dose-response curves of the unknown and standard materials are both linear and parallel. Later Harte (*2*) demonstrated that each formula was reducible to a single line which, under the conditions of that test, could be used for a rapid graphic determination of the percentage potency. This was a distinct improvement over the use of radial lines employed by Knudsen (*3*), but still left much to be desired, since the position of the line varied with the two parameters: C, the log ratio of the concentration of the unknown to that of the standard, and d, the log interval between the successive doses of both the unknown and standard. Harte, however, avoided the second parameter by the use of a fixed d and established a

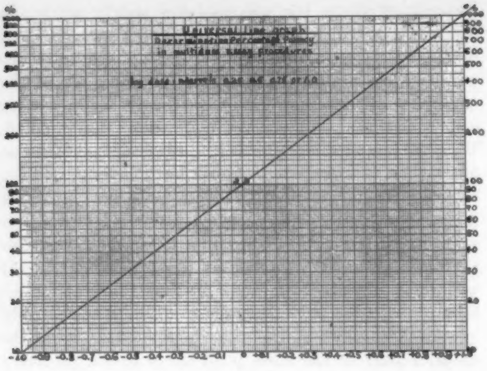

FIG. 1.

family of parallel lines, the position of which was determined by C.

It occurred to the author that if a single line could be drawn that would have universal applicability to all assays in which the requirements of linearity and parallelism were met, it should prove extremely useful. Such a condition of universal applicability within the limits of 10–1,000% would be met if in the basic formula, Percentage potency $=[\text{Antilog } 2.0 \pm C \pm kdP]$,[1] the concentration ratio, C, were omitted and kd were always some simple multiple of 1.0. Then on semilogarithmic paper[2] (Fig. 1) a line drawn diagonally from the 1 in the lower left-hand corner to the 1 in the upper right-hand corner would pass through 2.0, i.e., 100% at the central perpendicular line zero. The heavy lines to the right of zero on the base line would then be labeled + 0.1, + 0.2, + 0.3 . . . . . + 1.0, and, similarly, reading from right to left, those at the left of zero would be labeled − 0.1, − 0.2 . . . . . to − 1.0. The figures on the perpendicular logarithmically divided lines in the right and left margins would in the lower cycle correspond to 10, 20, 30 . . . . . 100%, and those in the upper cycle to 100, 200 . . . . . 1,000%.

To determine the percentage potency graphically one follows 6 simple steps: (1) the replicate observations for each dose level of standard and unknown are summed; (2) corresponding levels of U and S values are inserted in the formula for P for the number of doses employed (Table 1); (3) the arithmetic processes involved in this formula are carried out; (4) the P value found is treated as indicated on the right-hand side of the table according to the dilution employed; (5) the figure obtained from the multiplication and/or division of the original P is used to enter the base line to the right or left of zero, depending upon the sign; and (6) by following the entry perpendicularly to its intersection with the line and then horizontally to the right- or left-hand margin, one is enabled to read the percentage potency directly. Although a family of parallel lines based upon different C values can be established as Harte suggested,

TABLE 1

USE OF P TO OBTAIN PERCENTAGE POTENCY ON UNIVERSAL LINE GRAPH

No. doses/ assay	k*	P	Dilution			
			1: 1.78	1: 3.15 or 1: 3.2	1: 5.6	1: 10
			Enter base line of graph at			
2	1	$\frac{(U_2+U_1)-(S_2+S_1)}{(U_2+S_2)-(U_1+S_1)}$	$P_{/4}$	$P_{/2}$	$3P_{/4}$	P
3	4/3	$\frac{(U_3+U_2+U_1)-(S_3+S_2+S_1)}{(U_3+S_3)-(U_1+S_1)}$	$P_{/3}$	$2P_{/3}$	P	$4P_{/3}$
4	5	$\frac{(U_4+U_3+U_2+U_1)-(S_4+S_3+S_2+S_1)}{[2(U_4+S_4)+(U_3+S_3)]-[2(U_1+S_1)+(U_2+S_2)]}$	$5P_{/4}$	$5P_{/2}$	$15P_{/4}$	$5P$
5	4	$\frac{(U_5+U_4+U_3+U_2+U_1)-(S_5+S_4+S_3+S_2+S_1)}{[2(U_5+S_5)+(U_4+S_4)]-[2(U_1+S_1)+(U_2+S_2)]}$	P	$2P$	$3P$	$4P$
7	8	$\frac{(U_7+U_6+U_5+U_4+U_3+U_2+U_1)-(S_7+S_6+S_5+S_4+S_3+S_2+S_1)}{[3U_7+S_7)+2(U_6+S_6)+(U_5+S_5)]-[3(U_1+S_1)+2(U_2+S_2)+(U_3+S_3)]}$	$2P$	$4P$	$6P$	$8P$

* These values may be inserted in basic formula, percentage potency = Antilog $[2 \pm C + kdP]$, to obtain potency with number of doses used. For example, in the 5-dose assay formula, as follows: Percentage potency = Antilog $[2.0 \pm C + 4dP_5]$. The use of this formula, however, necessitates the finding of the antilog from tables of logarithms.

d = log dose interval. U and S refer to unknown and standard, respectively, and subscripts represent dose levels, larger subscripts denoting greater concentrations.

the author feels that the ratio of concentration of unknown to standard can best be handled by a separate multiplication or division of the percentage value obtained graphically.

It will be noted that in Table 1, P for the 6-dose assay is omitted. This is because k for the 6-dose assay

[1] P is used in the sense in which Harte employed it and represents the fraction referred to in Sherwood's original paper, P_2 being P for a 2-dose assay, and P_5 that of a 5-dose assay (Table 1); 2 is the logarithm of 100%; k is a parameter which varies according to the number of doses used in the standard and the unknown; and d is the log-dose interval.

[2] Semilogarithmic paper, 2-c, short side × 20 to the in., K & E No. 359 64, is used.

TABLE 2

EFFECT ON PERCENTAGE POTENCY—PRECISE DILUTIONS VS. SIMPLE DILUTIONS

Precise dilution	Log-dose interval	Simple dilution	Log-dose interval	Percentages obtained by precise dilution			
				10%	66.67%	150%	1,000%
1:1.7783	0.25000	1: 1.78	0.25042	9.96	66.62	150.10	1,003.88
1: 3.1623	0.50000	1: 3.15	0.49831	10.08	66.76	149.80	992.20
		1: 3.2	0.50515	9.77	66.39	150.63	1,024.00
1: 5.6234	0.75000	1: 5.6	0.74896	10.06	66.73	149.82	994.45

Calculations were made by substitution in the 2-dose assay formula in which $\pm C$—i.e., log concentration relationship between standard and unknown—has been omitted. Formula then reads Percentage potency = Antilog $[2.0 \pm dP_2]$. 2.0 = log 100, d = log successive dose intervals, and $P_2 = \dfrac{(U_2 + U_1) - (S_2 + S_1)}{(U_2 + S_2) - (U_1 + S_1)}$

With dilution of 1 : 1.7783 log-dose interval = 0.25000. Log of 10% = 1.0 ; hence, by substitution, formula becomes Percentage potency = Antilog 2 + 0.25000(−4), whereas when 1 : 1.78 used, log-dose interval = 0.25042, and formula reads Percentage potency = Antilog 2 + 0.25042(−4), or Antilog 0.99832 = 9.9613%.

is 35/3, and the use of such a figure is inefficient. Although it is not very likely that the 7-dose assay would be used routinely, its P was included for the sake of completeness. It is possible that one might wish to include a larger number of dose levels on an unknown, in which case if necessary one could discard some levels at either or both ends if the limit of linearity of the dose-response curve was exceeded. Percentage potency would then be calculated on the doses of unknown remaining plus an equal number of corresponding doses of the standard.

Table 2 gives a comparison of results obtained when simple dilutions of 1:1.78, 1:3.15 or 1:3.2, and 1:5.6 replace the precise dilutions of 1:1.7783, 1:3.1623, and 1:5.6234. It should be noted that at 100% the error is zero. Since the errors at the ends of the curve are so slight in comparison with the errors inherent to the assay methods, the use of the simpler dilutions in routine tests is suggested.

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Potassium Excretion in Rats

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There is evidence that potassium is filtered through the glomeruli and reabsorbed partially by the tubules, in normal man (*1, 2*), dog (*3*), and rat (*4*). It has recently been suggested, however, that in certain circumstances potassium may also be secreted by the tubules; this was shown in anesthetized dogs during "forced osmotic diuresis" with urea (*5*), in unanesthetized dogs after administration of salyrgan or intravenous injection of a hypertonic solution of potassium chloride (*6*), and in human beings suffering from severe renal insufficiency (*7*).

When investigating the mechanism of sodium and potassium excretion in rats (*4*) a few cases in which the potassium clearances were found to be higher than that of inulin were deliberately discarded: they were (*a*) animals which in spite of the administration of 5% of their body weight of water had an abnormally low urine flow, probably as a result of accidental dehydration, and (*b*) rats in which the rate of urine flow was so high that a faulty measurement of the urine volume was assumed. It is known that under both circumstances there is a release of intracellular potassium resulting in an increase of the plasma potassium concentration. In two rats, where the urine flow amounted to .0010 and .0015 ml/100 g/min only, the ratio potassium clearance/inulin clearance was 1.1 and 1.3, respectively; similar results were found in two other animals with an extremely high rate of urine flow: .1070 and .1062 ml/100 g/min. In these cases, values for T_K (= amount of K reabsorbed expressed as percentage of that filtered [*4*]) were negative, indicating that some potassium had been secreted by the tubules and added to the glomerular filtrate.

These findings suggested to Heller (*8*) an interesting interpretation of some previous results (*9*) : Heller had found that after 24 hr of dehydration the amount of potassium excreted in the urine was increased by 35% in adult rats, but decreased by 54% in newborn animals. As no evidence of a significant decrease in the glomerular filtration rate could be shown in these adult dehydrated animals, it would seem likely, from the above results, that the enhanced potassium excretion was the result of a tubular secretion of that ion. Such secretion, however, did not seem to occur in newborn rats, in which the depression of glomerular filtration seems to be the principal factor regulating the renal excretion of potassium (*2*).

This discrepancy between the tubular function of adult and newborn rats is in line with results of two independent series of investigations carried out recently in this department. It could be shown that the urine flow of newborn rats remains unaffected after the administration of either diuretics (Dicker, unpublished) or vasopressin (Heller, unpublished). The lack of sensitivity of the tubules of newborn rats to pharmacological and physiological stimuli (*10*) is thus

in sharp contrast to the highly developed adaptability of tubules of adult animals.

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Silver Nitrate as a Test for Ortho and Para Dihydric Phenols

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On attempting to prepare salts of the two plant pigments, osajin and pomiferin (*1*), it was observed that the latter reacted with neutral silver nitrate in alcoholic solution to deposit a silver mirror and yielded a gold-colored solution, whereas the former under the same conditions gave no reaction. Further investigation of this behavior demonstrated that in general those aromatic compounds containing two or more phenolic hydroxyl groups, which were ortho or para to each other, readily reacted with neutral silver nitrate, whereas those having a single phenolic hydroxyl group, or two or more hydroxyl groups meta to each other on an aryl nucleus did not react. Substances which formed insoluble silver salts in the alcoholic solution did not give a positive test even though they possessed the requisite structural features.

The test solution of silver nitrate was made up by dissolving 1.0 g of silver nitrate (analytical grade) in 8.0 ml of distilled water. The test was carried out by dissolving 5–10 mg of the compound in 5.0 ml of 95% ethanol in a clean test tube. Three drops of the silver nitrate test reagent was added, and the solution was shaken for 15 min. It was then observed for the presence of a silver mirror and coloration. If a negative or very faint test was apparent after 10 min of shaking the test tube was warmed on a water bath at 60° for 1 min.

The results for the various compounds tested are listed in Table 1. Rutin did not give a positive test even after it was warmed on the water bath. Also, quercetin did not give a positive test but appeared to form an insoluble precipitate. Both these substances possess 2 phenolic hydroxyl groups located ortho to one another on an aryl nucleus and the results are in agreement with those previously reported by Schunck (*2*) and Weiss (*3*).

TABLE 1

COMPOUNDS TESTED WITH NEUTRAL SILVER NITRATE

Compound	Results
Osajin	No reaction, even on warming
Pomiferin*	Silver mirror; gold-colored solution; no warming necessary
Iso-osajin*	No reaction, even on warming
Isopomiferin*	Silver mirror; gold-colored solution; warming necessary
Iso-osajin monomethyl ether*	No reaction, even on warming
Isopomiferin dimethyl ether*	" " " " "
Dihydro iso-osajin*	" " " " "
Dihydro isopomiferin*	Silver mirror; gold-colored solution; no warming necessary
3′,4′,7,8-Tetrahydroxy flavanone*	Silver mirror; gold-colored solution; no warming necessary
Narigin*	No reaction, even on warming
Eriodictyol*	Silver mirror; gold-colored solution; no warming necessary
Homoeriodictyol*	No reaction, even on warming
Rutin†	No mirror formed; solution a salmon color after warming
Quercetin*	No mirror formed; precipitate observed; no further change on warming
Phenol	No reaction, even on warming
Catechol	Silver mirror; red solution; no warming necessary
Hydroquinone	Silver mirror; gold-colored solution; no warming necessary
Phloroglucinol	No reaction, even on warming
Tetrabromocatechol	Silver mirror; gold-colored solution; no heating necessary
Pyrogallol	Silver mirror; red-colored solution; no heating necessary
o-Hydroxyphenyl benzyl ketone	No reaction, even on warming
2,4-Dibenzyloxy-1,3-dimethoxy benzene	No heating, even on warming

* The author is indebted to M. L. Wolfrom for samples of these compounds.

† The author is indebted to S. B. Penick and Co., New York, for a sample of this compound.

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Comments and Communications

Dr. Langmuir's Article on Precipitation Control

In his article entitled "Control of Precipitation from Cumulus Clouds by Various Seeding Techniques" (*Science,* **112**, 35 [1950]), Dr. Langmuir states that the results of silver iodide seeding in New Mexico on October 14, 1948, and July 21, 1949, seem to him to "prove conclusively that silver iodide seeding produced practically all of the rain in the State of New Mexico on these two days." Because of the widespread public interest in the possibility of artificially controlling precipitation, and the economic implications which would follow from successful experiments of the scale noted in the article, Dr. Langmuir's statement should be subjected to a careful examination. It will therefore be interesting to examine closely the methods by which he arrives at his conclusion.

Three main arguments appear to be used in the analysis: (1) the similarity or correlation between the patterns of rainfall over the state of New Mexico on October 14 and July 21; (2) the closeness of fit of each of these patterns to the hypothesis that the rainfall should be a maximum in the vicinity of the seeding point and thence decrease outward; and (3) that the time of beginning of rainfall on July 21 became progressively later in the day as the distance from the seeding point increased and fitted closely the travel time of the silver iodide based on observed winds.

Using these three approaches, and making computations from the rainfall data of the region on the two days in question, Dr. Langmuir obtains extraordinarily high probability figures, suggesting that the patterns observed could not have occurred as a consequence of natural causes. These probabilities are computed on the assumption that the rainfall values for the subareas into which he divides the state can be treated as so many independent random numbers.

The main difficulty with this type of analysis is that in actual weather situations the distribution of rainfall is not purely random, and that adjacent areas are not independent of one another. The occurrence of rainfall depends upon many factors, such as the moisture content of the air, the convergence of the air flow at various heights, the presence of air-mass discontinuities, and the topography of the ground, to mention several. Since these quantities are neither separately nor jointly distributed at random over a region on a particular day, it is equally true that the areal distribution of rainfall is not random.

It therefore appears that it would be necessary to find out what the true distribution of correlations between rainfall patterns actually is before stating that the correlation on the two days in question was much higher than would occur naturally, and therefore indicated significant results. Rainfall records have been taken at many stations in New Mexico for many years, and it is thus possible to examine these records and determine the natural frequency of occurrence of patterns similar to Dr. Langmuir's or to any other particular pattern. Then, having established what is normally to be expected in the way of rainfall patterns, those patterns occurring on the two seeding days can be studied to see whether they departed significantly from the normal.

As an example of the type of analysis in such cases, William Lewis, of the Weather Bureau, who was attached to General Electric's Project Cirrus with which Dr. Langmuir is associated, divided the state of New Mexico into 30 areas of approximately equal size by using even degrees of latitude and longitude. Eight two-day rainfall periods were selected at random from a list of cases in which rainfall occurred at at least 125 stations within the state. Rainfall quantities similar to those used by Dr. Langmuir were obtained for each of the 30 areas for each of the eight days, and all possible (28) correlations between the patterns on the different days were obtained. The correlation between the patterns on Langmuir's two seeding periods was also calculated—using the rainfall on October 14–15 versus that on July 21–22—and it came out to be 0.45. Of the 28 values obtained from the random sample, three were numerically greater than on the seeding days, with two others almost as high. With little effort it was also possible to pick out two other periods (July 4–5, 1945, vs. August 24–25, 1946) where the patterns were much more similar than on the seeding days, the correlation coefficient being 0.77.

This analysis would seem to indicate that it is not particularly unusual to encounter rainfall periods in New Mexico in which the patterns bear considerable similarity. Thus it would appear that the similarity noticed between the patterns on the two seeding occasions has little, if any, significance. The differences which might be expected from using a somewhat different choice of areas, and of using two-day instead of one-day rainfall, are not considered to be critical. The correlations, both for the seeding days and for the past data, would presumably be larger when fewer areas were used, and vice versa. For instance, the correlation between October 14 and July 21, using data from individual stations, is .02, or essentially zero.

It would be equally simple to determine the frequency of occurrence of particular patterns following Dr. Langmuir's hypothesis that they should be related to the position of the seeding generator, or of the occurrence of rainfall patterns which move in particular directions. Since Dr. Langmuir has not made such analyses, however, it is not clear how he can determine the probability that the behavior of the rain on the seeding days was so abnormal.

It will be recalled that as a result of his analysis

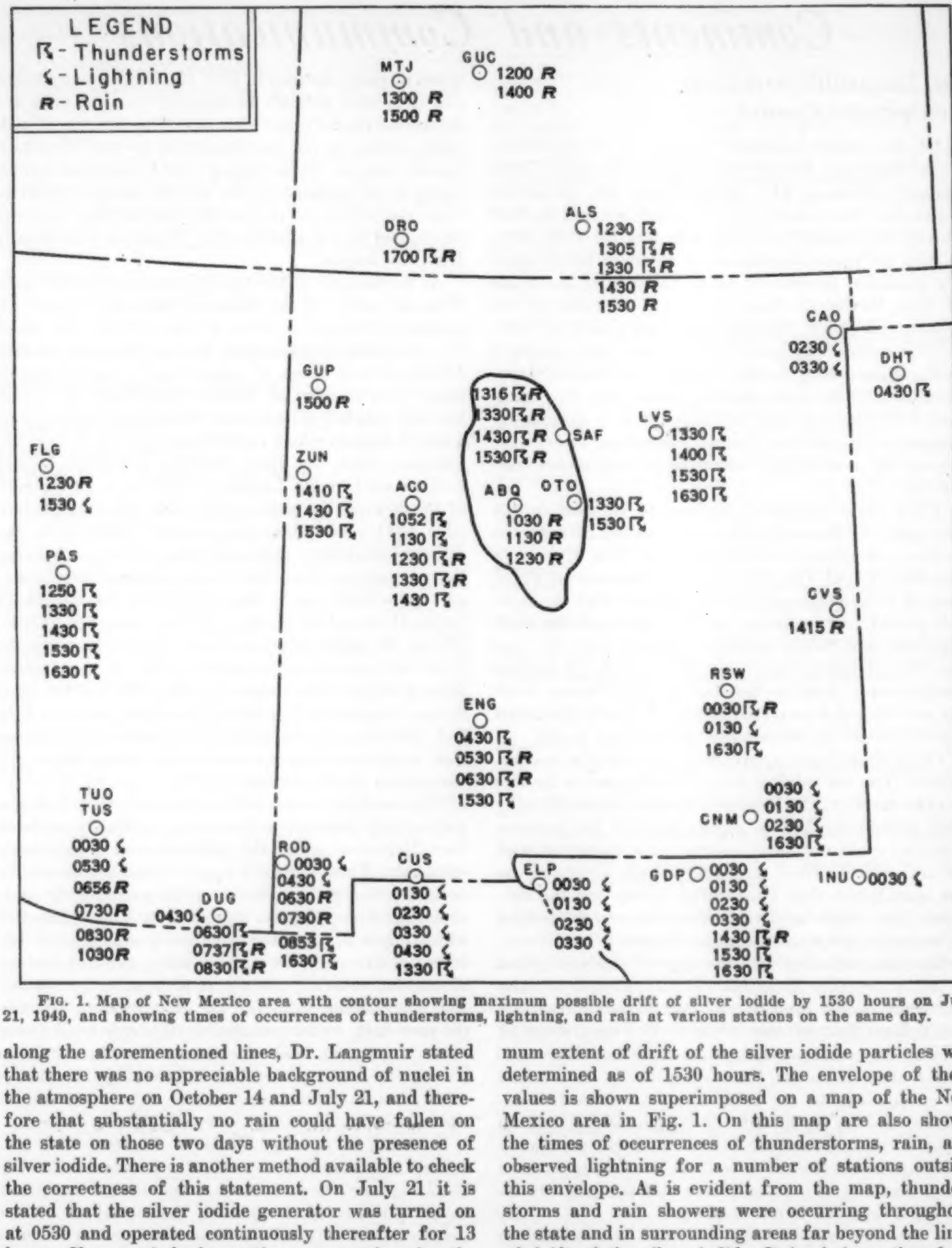

FIG. 1. Map of New Mexico area with contour showing maximum possible drift of silver iodide by 1530 hours on July 21, 1949, and showing times of occurrences of thunderstorms, lightning, and rain at various stations on the same day.

along the aforementioned lines, Dr. Langmuir stated that there was no appreciable background of nuclei in the atmosphere on October 14 and July 21, and therefore that substantially no rain could have fallen on the state on those two days without the presence of silver iodide. There is another method available to check the correctness of this statement. On July 21 it is stated that the silver iodide generator was turned on at 0530 and operated continuously thereafter for 13 hours. Upper wind observations were taken by the Weather Bureau at Albuquerque (about 10 miles from the generator) at 0800, 1100, and 1400 hours on that day. Using the most favorable combinations of winds reported from the surface up to 20,000 ft, the maximum extent of drift of the silver iodide particles was determined as of 1530 hours. The envelope of these values is shown superimposed on a map of the New Mexico area in Fig. 1. On this map are also shown the times of occurrences of thunderstorms, rain, and observed lightning for a number of stations outside this envelope. As is evident from the map, thunderstorms and rain showers were occurring throughout the state and in surrounding areas far beyond the limit of drift of the silver iodide. It is obvious, therefore, that it was quite possible for rainfall to have occurred naturally on the day in question.

It would be possible to examine the weather situation on these two days even more closely, and to point

out natural factors that would lead to the similarity in rainfall that Langmuir detects on the two days. If days from the past records on which the weather situations were equally similar had been chosen for establishing the frequency of pattern correlations, the expected correlation would have undoubtedly been much higher than in the example presented above.

It is generally accepted that the seeding of clouds with dry ice or other agents has the effect of converting supercooled water droplets into ice crystals. Photographs of the trenches and holes cut in stratus clouds present very striking spectacles. The value of this discovery and its usefulness in studying the physics of clouds are not to be underestimated. Many observers have also noted that small amounts of precipitation begin to fall from the cloud bases below the paths of the seeding airplanes soon after the planes have completed their seeding runs. In most cases, however, it appears that this precipitation evaporates before reaching the ground. In many other cases observers have noted that seeding causes the clouds to dissipate and thus seems to inhibit the possibility of rain.

Although there are a few cases where visual observations suggest that the precipitation may have been affected as the result of seeding clouds with dry ice or silver iodide, there is as yet no conclusive proof that this actually occurred. And the further question as to how much of the rainfall would have fallen naturally is even more in doubt. Regarding those claims of success in increasing the rainfall, the majority appear to be based upon cases where the rain has occurred primarily, if not entirely, as a result of natural causes. Carefully controlled experiments under various meteorological conditions, and over considerable periods of time, will be required to permit sound conclusions as to the quantity of usable rainfall that may be expected to result from cloud seeding.

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AT VARIOUS times during the past year certain periodicals, both technical and popular, have devoted considerable attention to the subject of rain making. Special mention has been made of two particular rain-making experiments carried out near Albuquerque, New Mexico, on October 14, 1948, and on July 21, 1949, by Irving Langmuir and a group of his associates from the General Electric Research Laboratory. Dr. Langmuir has claimed (*Science*, **112**, 35 [1950]) that these experiments produced copious rainfalls over very large areas. More recently the daily press (New York *Times*, Oct. 13, 1950, e.g.) has reported a statement made by Dr. Langmuir at the Schenectady meeting of the National Academy of Sciences to the effect that the abnormally large amounts of rainfall that occurred in the Mississippi Valley last winter appear to have been caused by the systematic release of silver iodide "smoke" at Socorro, New Mexico, during that period.

Several months ago the undersigned were afforded the opportunity of discussing at some length with Dr. Langmuir the various circumstances and details surrounding these particular experimental operations, and of examining the evidence put forward by him as proof of success in making rain on a large scale. Subsequent to this meeting we were asked by the president of the American Meteorological Society to prepare an informal report based on the results of the conference. Our conclusions are summarized in the following paragraphs.

In the first place, it should be emphasized that the formation and coalescence of atmospheric ice and water particles are as yet only imperfectly understood, despite recent great advances, which are due in large measure to the investigations of Langmuir, Schaefer, and their co-workers. At present it is still impossible to deduce conclusively from purely physical reasoning the complete future sequence of events if a given quantity of silver iodide "smoke" is introduced into a cloud whose meteorological parameters are known. Furthermore, there may be a limit to the length of time in which silver iodide remains efficient as a cloud-seeding agent when it is exposed to solar radiation. Since the limit does not yet appear to be definitely known, it seems impossible to state with certainty the distances to which this material will retain its effectiveness when carried along in the atmosphere. For these reasons, and because of the impossibility of controlling the atmosphere so as to permit a precise prediction of the weather that would occur if no attempt at cloud modification were made, it is extremely difficult to evaluate claims of success in rain making.

There are two possible approaches to the problem of determining the effect of cloud seeding on rainfall, both of which involve thorough study if any satisfactory objective judgment is to be achieved. One approach is to estimate the amount of rain that might be expected to fall naturally under the meteorological conditions prevailing at the time of a particular experiment. In this respect it can be said that at the time of the two experiments near Albuquerque the broad-scale weather pattern was quite favorable to the natural development of the thunderstorms and moderately heavy rainfall that occurred in both instances. However, a satisfactory quantitative estimate of the naturally occurring rainfall would have to be based on the results of a number of carefully controlled experiments, conducted under a variety of weather conditions. Since sufficient data of this kind have not yet been accumulated, it cannot be determined to what extent the future weather development may have been altered by artificial initiation of precipitation, nor is it possible to decide how much, if any, of the rainfall that occurred at individual points surrounding the site of the experiments in question should be attributed to cloud seeding.

In the case of the heavy rainfall over the Mississippi Valley in the winter of 1949, it is even more difficult to judge the effect of cloud seeding on the over-all weather pattern. Even if silver iodide does remain an efficient seeding agent for long intervals and over large distances, it is virtually impossible to evaluate the horizontal and vertical transport, and, hence, the contingent distribution and concentration of the silver iodide through the atmosphere when the distances involved are as great as those between New Mexico and the Mississippi Valley. On the other hand, it can be said with certainty that the patterns of weather and rainfall over the United States during this period were quite similar to a number of corresponding periods in the past, and that they fit very naturally and normally into the rather unusual Northern Hemisphere weather pattern of that period. To anyone who is fully aware of the world-wide character of the mechanics of the large-scale wind systems and of the apparently secondary and incidental role of rainfall distribution in the world-wide meteorological pattern, the implication that the purported artificial production of precipitation in the Mississippi Valley significantly modified this pattern seems fantastic. It is impossible, however, either to verify or to disprove Langmuir's contention in this respect from his analysis of the data as presented to us.

The other approach to the problem of determining the effect of cloud seeding on rainfall is primarily statistical. In the case of the Albuquerque experiments such an approach involves a careful consideration of the striking similarity of the rainfall patterns during the two days on which the allegedly successful experiments were conducted, particularly an investigation of the odds against the occurrence of such a degree of similarity by chance alone. In order to accomplish a reliable determination of these odds, a complete analysis of the entire situation should be made, starting with an objective analysis of original data pertaining to moisture distribution, winds, and rainfall in relation to topography. (Topography alone could be expected to produce a certain similarity in precipitation patterns on different days.) In addition, it would be necessary, because of the amount of serial correlation that occurs in weather patterns, and also the similarity that oftentimes exists between patterns, to determine from a study of climatological records what are the probabilities of such an occurrence of agreement between patterns. As far as we have been able to discover, however, these necessary statistical precautions were not taken in the original analysis of the two Albuquerque experiments. Therefore, we cannot accept as proved the odds against chance occurrence that have been cited by Langmuir. It is our considered opinion that the artificial production of substantial amounts of rainfall over an area of the order of 100,000 square miles definitely has not been demonstrated in these two cases.

A similar statistical approach must be made in order to achieve an effective evaluation of the high correlation between the days on which silver iodide "smoke" was released at Socorro, New Mexico, and the subsequent occurrence of rainfall in the Mississippi Valley. On the basis of a purely random situation this high correlation between the release of silver iodide and the rainfall probably is significant, but because of the general statistical behavior of rainfall patterns the situation in question should be carefully compared with the behavior of previous cases of abnormally heavy winter rainfall in that vicinity to see whether the periodicity exhibited in the present case is a likely occurrence by pure chance. Since, to the best of our knowledge, such a comparison has not yet been undertaken by Dr. Langmuir, we cannot accord credence to the sweeping inference that the abnormal character of the basic weather pattern was the result of the silver iodide operations at Socorro.

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News and Notes

Scientists in the News

Thomas Page Anderson, of the Mayo Foundation, has been appointed director of the department of physical medicine for the new Medical Health Center at Ohio State. The appointment is effective April 1. Dr. Anderson, who has been a fellow in physical medicine at Mayo since January 1948, will direct the work in the new center concerned with the rehabilitation of chronic medical and post-traumatic and post-surgical patients. He succeeds **Shelby Gamble**, who resigned to go to the Cleveland Clinic. In the interim, the acting director is **Richard H. Jacques.**

Wallace W. Atwood, Jr., has been appointed executive secretary, Division of International Relations, National Academy of Sciences–National Research Council. He will have responsibility for the activities of the joint organization in international scientific relations, under the direction of Roger Adams, foreign secretary of the academy and chairman of NRC's Division of International Relations. Dr. Atwood will be liaison officer with the Office of the Science Advisor, Department of State, and will represent the NRC in matters pertaining to international scientific unions, Unesco relations, international exchange of scientific literature, and similar activities. He was formerly with the RDB Committee on Geophysics and Geography.

Connecticut Supreme Court Justice **Raymond E. Baldwin** has been appointed to the Board of Control of the Connecticut Agricultural Experiment Station succeeding **Edward C. Schneider**, professor of biology at Wesleyan University, who recently retired after 31 years of service. The appointment comes from Wesleyan University, of which Judge Baldwin is an alumnus. Under the station charter, the responsibility of appointing one member of the station's Board of Control rests with Wesleyan. Other appointments come from the Sheffield Scientific School, the University of Connecticut, and the Governor. In addition, the Governor, the Commissioner of Farms and Markets, and the Director of the Station are members ex officio.

Visitors at the Bureau of Standards during the past few weeks included: **Lars Bjellerup**, Department of Organic Chemistry, University of Lund, who has joined the National Bureau of Standards as a guest worker in its Thermodynamics Section for six months; **Robert F. Legget**, Division of Building Research, National Research Council of Canada, Ottawa; **Harald A:son Moberg**, Swedish Government Agricultural Machinery Testing Institute, Uppsala; **Jan C. Stryland**, Van der Waals Laboratory, Amsterdam; **Leonardo Villena**, Instituto de Optica "Daza de Valdes," Madrid; **J. S. Foster**, Department of Physics, McGill University, Montreal; **Sigeiti Moriguti**, University of Tokyo; **J. A. Haring**, Laboratory of N. V. Philips Co., Eindoven; **Taro Tanaka**, Technical Research Institute, Ministry of Transportation, Tokyo; **Yutaka Tanaka**, National Hygienic Laboratory, Tokyo; and **G. E. Tummers**, State Mines, Netherlands.

Gösta Brown, Stig Lublin, and **Per Norbäck**, of the Royal Institute of Technology, University of Stockholm; **G. C. Chaterji**, Geological Survey, Calcutta; **John M. Dodds**, Metropolitan-Vickers, Manchester, Eng.; **Cayaid Ener**, University of Istanbul; **J. C. R. Heydenrych**, National Physical Laboratory, Pretoria; and **M. Tomota**, Yokogawa Electric Works, Tokyo, were other recent visitors at the Bureau of Standards. **Andre Juliard**, professor of chemistry of the University of Brussels, who is currently with the University of Pennsylvania as an exchange professor, also visited the Bureau.

Charles M. B. Cadwalader has announced his retirement as president of the Academy of Natural Sciences of Philadelphia. His successor, **M. Albert Linton**, is the nineteenth president of the Academy since its founding in 1812. Mr. Cadwalader will continue as a member of the board. He has been active in the direction of the academy for nearly 25 years, 13 of which he served as president.

Eugenie Clark, who is working at the Marine Biological Station at Ghardaqa, Red Sea, Egypt, as a Fulbright scholar, has been appointed a research associate in the Department of Animal Behavior of the American Museum of Natural History.

Howard S. Coleman, head of the Optical Research Laboratories at the University of Texas, has become director of Bausch & Lomb Optical Company's Scientific Bureau. Dr. Coleman graduated from Penn State in 1938, and earned his doctorate there in physics while serving as an instructor. Since then he has specialized in optics at Frankford Arsenal (Philadelphia), Penn State, and the University of Texas, where he was in charge of the optical laboratories and teaching programs in optics.

Jean A. Curran has been appointed dean of the State University College of Medicine in New York City. Dr. Curran was president of the Long Island College of Medicine until that school was merged last April with the State University to form the State Medical School. **Duncan Clark**, who was dean of the former Long Island College, has been made professor of environment medicine and community health. The New York City unit is one of two state university medical colleges. The other is at Syracuse University.

G. Brooks Earnest, professor of engineering surveying at Case Institute of Technology, has been named dean of the Fenn engineering school, and **Adrian D. Joyce**, chairman of the board of the Glidden Company, has been elected to the Fenn board of trustees. Professor Earnest, consulting director of the Cleveland Geo-

detic Survey, a director of the American Society of Civil Engineers and of the Cleveland Society of Professional Engineers, succeeds **S. M. Spears.**

Robert F. Field has retired from the General Radio Company Engineering Department after 21 years of service. He was formerly a member of the faculty of Harvard University.

Richard Foster Flint, professor of geology at Yale, left February 2 for Europe to lecture on recent developments in Pleistocene research, at the universities of Cambridge, London, and Paris, and the Geological Society of London.

John F. Fulton, Yale physiologist, has been named to fill the newly created position of Sterling professor of the History of Medicine. He will continue with certain phases of his physiological research.

R. Ruggles Gates, of The Biological Laboratories, Harvard, was recently elected a life fellow of the Royal Society of Arts (London) and an honorary member of the Botanical Society of Japan (Tokyo).

Donald Lincoln Herr has been appointed head of the Section for Guided Missile Research and Development —Production Coordination, and also member of the Advisory Council of the Research and Development Laboratories, Hughes Aircraft Company, Culver City.

Shu Chu Shen has been appointed assistant research professor of medicine at Tufts College Medical School. He will continue his cancer research work in hematology at the Holy Ghost Hospital, Cambridge, as a senior Damon Runyon research fellow. **George Meissner,** formerly at McGill University, Department of Pathology, has been appointed assistant professor of pathology at Tufts, research associate in the Tufts Cancer Research and Cancer Control Unit, and pathologist of the Jewish Memorial Hospital in Roxbury, Mass.

G. L. R. von Koenigswald, discoverer of the Java ape man and professor of paleontology at the University of Utrecht, has gone to South Africa to study the ape-man fossils, and is working with **Robert Broom** at the Transvaal Museum.

Russell M. Wilder has been appointed director of the recently established National Institute of Arthritis and Metabolic Diseases of the Public Health Service. **Floyd S. Daft** will be associate director of the new institute. Dr. Wilder retired December 31 as head of the Department of Medicine of the Mayo Foundation and senior consultant in medicine of the Mayo Clinic.

Richard J. Winzler, professor in the Department of Biochemistry and Nutrition at the University of Southern California, is spending six months of his sabbatical leave at the University of Wisconsin as visiting research professor in the Department of Physiological Chemistry.

Fellowships

Angel Ramos, editor and publisher of *El Mundo,* San Juan daily newspaper, has established a $1,000 scholarship at the **Columbia University School of Journalism** for a Puerto Rican student. Ramos established the scholarship with the prize money he received in 1950 as recipient of a Maria Moors Cabot journalism award.

The **Bausch & Lomb Honorary Science Awards** program will be administered for the eighth consecutive year by the University of Rochester. Science pupils in nearly 5,000 secondary schools will compete for scholarships having a maximum value of $3,200 each. Twelve or more will be selected as finalists, from whom three winners will be chosen. Applications should be filed with the University of Rochester by *March 10.*

Seventy-eight postgraduate and postdoctoral fellowships in 47 universities and grants-in-aid to ten universities, in the amount of $390,400, will be awarded by **E. I. du Pont de Nemours** for the academic year 1951–52. The fellowships will cover various scientific fields, and the grants-in-aid will provide $10,000 to each university for unrestricted use in fundamental chemical research. The ten universities are Caltech, Cornell, Harvard, Illinois, MIT, Minnesota, Ohio State, Princeton, Wisconsin, and Yale.

Sloan Fellowships for advanced study in economics and business administration at MIT will be awarded to fourteen young business executives. Awards range up to $3,720, and sponsorship by the employer is prerequisite. Applications must be made by *February 24* to Gerald B. Tallman, Executive Development Program, MIT, Cambridge 39, Mass.

The Vassar Plant Science Department is offering the **Helen Gates Putnam Graduate Fellowship in Conservation** for candidates who wish to work in the fields of microbiology, ecology, or plant physiology. For application blanks (returnable by *April 1*), write to Gladys E. Baker, Department of Plant Science, Vassar College, Poughkeepsie, N. Y.

Grants

The **Mount Desert Island Biological Laboratory,** Salisbury Cove, Maine, has received a grant of $10,000 from the Heart Institute of the USPHS. The grant will be used to further the work of training young investigators in the field of renal and cardiovascular physiology.

Utah State Agricultural College has received a USPHS grant of $50,220 for the study of insecticide residues in animal food products following their application to forage crops and subsequent consumption by animals. The project is under the direction of Clyde Biddulph.

Bernard Longwell, professor in the Department of Biochemistry, University of Colorado School of Med-

icine, has been awarded a USPHS research grant of $12,425 for the study of the effect of diabetes mellitus on the processes of reproduction.

The **Sugar Research Foundation** has given the Harvard School of Public Health a grant-in-aid for the study of sugar as the base for emergency rations for civilian populations. Six other laboratories that will share in the $146,835 appropriated for research this year by the foundation are at Emory University, Jefferson Medical College, Boston City Hospital, University of Pennsylvania School of Medicine, California Foods Research Institute, and Belmont Chemical Sales Development Co.

The **New York Zoological Society** has made a grant of $4,000 a year for three years to the Marine Biological Laboratory, Woods Hole, Mass., in support of a new course in marine ecology. Open to graduate students, the new course will begin this year.

The Cancer Research Institute of the Hospital de Enfermedades de la Nutrición, of Mexico City, has received a grant of $5,000 from the **Damon Runyon Fund** for research in the use of steroid drugs in the treatment of cervico-uterine cancer. A $10,000 gift to the same group was made by the Mexican hormone-manufacturing firm **Syntex, S. A.** Both grants were announced during the First International Symposium on Steroids in Clinical and Experimental Practice, held in the Mexican capital January 15.

The **Catherwood Foundation**, of Bryn Mawr, will provide funds to the Department of Limnology of the Academy of Natural Sciences, Philadelphia, to perfect a method for continuous scientific reading of the condition of any given stream, by means of a device which the academy is developing. Ruth Patrick is in charge of the limnological research.

New grants totaling $86,000 have been made by **Research Corporation** to support basic research in academic institutions. A special grant was made to the National Research Council for the publication of the *International Tables of Crystallographic Data.*

In the Laboratories

Brush Development Company has acquired the Faxfilm Company, of Cleveland, in a move to expand its line of surface-measuring instruments. Faxfilm is a process in which an exact reverse replica of a surface is made in clear plastic and projected in a micro-projector to give a three-dimensional effect. Tool scratches have been recorded down to a furrow 6/1,000,000 of an inch deep. R. W. Cook, former president of Faxfilm, will be associated with Brush Development.

Sterling-Winthrop Research Institute has made the following additions to its research staff: Clifford H. Casey, William B. Dickinson, Alice E. Fruehan, William T. Hunter, Maurice C. Olivier, John C. Seed, Burnett C. Southworth, Miriam L. Thompson, and John M. Winton.

Du Pont is constructing a new $2,700,000 laboratory-farm near Newark, Del., for a study of the control of bacterial and virus diseases, parasites and insects, and animal nutrition. Named for Charles M. A. Stine, retired Du Pont chemist, the farm is expected, by means of laboratory research, to produce improved medicines and food for animals.

The first industrial research unit in Latin America, the **Mexican Institute of Industrial Research**, has been organized as the outgrowth of a technological audit conducted by Armour Research Foundation. The new institute, which is sponsored by the Bank of Mexico and the Nacional Financiera, is located in the Loma Hermosa district of Mexico City, where it occupies 15,000 square feet of floor space. Among current projects is a search for a fuel to replace wood charcoal. Studies on the dehydration and storing of tortilla flour have resulted in the solution of a major problem of production and distribution. Mais Industrializado, S. A., in which the Mexican government has invested 3 million pesos, will soon be producing 100 tons of dehydrated flour daily. Milton E. Nelson, assistant director of the International Division of Armour Research Foundation, is director of laboratories at the institute and in charge of all technical research.

Sponsored by more than twenty corporations, representing oil, roofing, molded products, sealing compounds, and allied industries, the **National Asphalt Research Center** was recently established at The Franklin Institute Laboratories for Research and Development in Philadelphia. Major efforts during the first year will be directed toward devising practical and scientifically correct methods for measuring elasticity, plasticity, viscosity, and adhesion to solid surfaces at various temperatures and rates of shear.

Meetings and Elections

The Eastern North American Region of the Biometric Society held its annual meeting in Chicago on December 27–29 jointly with the Biometrics Section of the American Statistical Association and the Institute of Mathematical Statistics. At the regional business meeting on December 29, the following officers were named for the year 1951: vice-president, Horace W. Norton; secretary-treasurer, Walter T. Federer; Members of the Regional Committee for the period 1951–53, Donald Mainland and H. L. Lucas. The scientific program consisted of ten sessions. On Wednesday, December 27, there were sessions on "Statistical Problems in Radiobiology" under the chairmanship of A. E. Brandt, with papers by Bruce Wallace, S. L. Crump, and H. B. Jones; on "Theory of Variance Components" under the chairmanship of W. J. Youden, with papers by S. L. Crump, W. G. Cochran, and J. W. Tukey; on "Precision of Measurements" under the chairmanship of W. E. Deming, with papers by C. Eisenhart, F. E. Grubbs, and J. C. Whitwell; and on "Sources of Morbidity Statistics" under the chairmanship of H. F. Dorn, with papers by A. B. Thompson, N. R. Deardorff, and T. Woolsey

and S. Collins. The sessions on Thursday were entitled "Statistical Methods in Pharmacology and Immunology," with L. Miller presiding, and papers by L. F. Knudsen and H. C. Batson; "Application of Variance Components," with G. W. Snedecor presiding, and papers by W. A. Hendricks, R. E. Comstock and H. F. Robinson, and J. M. Cameron; and "Sample Survey Techniques," with W. F. Callander presiding, and papers by D. S. Robson and A. J. King, F. E. McVay and H. Tucker, and R. L. Anderson and A. L. Finkner. The sessions on Friday were "Statistical Methods in Medicine" under the chairmanship of H. Muench, with papers by E. Fix and J. Neyman, D. Mainland and J. W. Hopkins, and J. L. Hodges; "Contributed Papers" under the chairmanship of Evelyn Fix, with papers by C. J. Maloney, I. J. Bross, O. Felsenfeld, and N. Mantel; and "Contributed Papers" under the chairmanship of R. Gage, with papers by L. D. Calvin, F. E. Satterthwaite, W. T. Federer, and M. E. Morgan, P. MacLeod, C. I. Bliss, and E. O. Anderson.

W. T. Federer, *Secretary-Treasurer*

The annual meeting of the three national petroleum exploration societies will be held at the Jefferson Hotel, St. Louis, April 23–26. This is the 36th annual meeting for the **American Association of Petroleum Geologists,** the 24th for the **Society of Economic Paleontologists and Mineralogists,** and the 20th for the **Society of Exploration Geophysicists.** Secretary of the Interior Oscar Chapman will deliver the principal address on Tuesday, April 24.

The **American Crystallographic Association** is holding its winter meeting at the National Bureau of Standards this week in connection with the fiftieth anniversary celebration of the Bureau.

The **American Institute of Mining and Metallurgical Engineers,** meeting in St. Louis February 19–22, will hold 80 separate meetings, at which 250 scientific papers will be presented in the various fields of mining and metallurgy.

At the joint meeting of the **Association for Computing Machinery** and the **Industrial Mathematics Society,** March 27–28, at Wayne University, Detroit, papers will be presented on both analog and digital machines and on their scientific, engineering, and business applications, together with a display of components.

Newly elected officers of the **International Council of Women Psychologists** are: president, Lillian G. Portenier; vice president, Mary Ford; and secretary-treasurer, Naomi Ekdahl.

The **Institute of Navigation** will hold its 1951 Eastern Regional Meeting March 8–9 at the Shoreham Hotel, Washington, D. C. Rear Admiral Leo O. Colbert, former director of the U. S. Coast and Geodetic Survey, will be general chairman.

Torrey Botanical Club, at its annual dinner at Hunter College, January 16, elected the following officers: president, A. E. Hitchcock; vice presidents, M. A. Johnson, and L. M. Black. P. W. Zimmerman and R. H. Cheney were elected AAAS Council representatives.

Deaths

John Robert Loofbourow, 48, professor of biophysics and executive officer of the Department of Biology at MIT, died suddenly on January 22. Dr. Loofbourow was executive secretary of the MIT Radiation Laboratory from 1942 to 1946, and special advisor to the Atomic Energy Commission in 1947 and 1948. For "outstanding services to his country," he received the President's Certificate of Merit in 1948. In addition to his departmental duties, he was serving as chairman of the faculty of MIT at the time of his death. Dr. Loofbourow was survived by his widow, **Dr. Dorothea G. Loofbourow,** a member of the staff of the Massachusetts General Hospital, by only a few days. She died February 1 at the age of 48.

Harald Bohr, Danish mathematician, and younger brother of Niels Bohr, died January 21 at the age of 63. He was professor at the University of Technology in Copenhagen for fifteen years, later becoming professor of mathematics at Copenhagen University. Dr. Bohr last visited the United States in 1950 during the meeting of the International Congress of Mathematicians at Harvard.

Daniel Buchanan, professor emeritus of mathematics and dean emeritus of the Faculty of Arts and Sciences of the University of British Columbia, died in Vancouver on December 1 at 70. A graduate student of F. R. Moulton, former AAAS Administrative Secretary, Dr. Buchanan was a specialist in mathematical astronomy and celestial mechanics.

A retired Agriculture Department entomologist and former associate curator of the National Museum's Insect Division, **James Chamberlain Crawford,** died recently at 70. He was a specialist on the Mexican bean beetle.

Anna Linder, well-known Swedish Red Cross nurse of World War I, died recently in Stockholm at the age of 77. For her war work she was made honorary doctor of medicine at Uppsala University.

Robert U. Patterson, Maj. Gen., ret., an honorary consultant to the Army Medical Library, died at Walter Reed General Hospital, Washington, D. C., December 6. He had been Surgeon General of the Army and dean of the medical schools of the universities of Oklahoma and Maryland.

Wilhelm Schüffner died recently at the age of 83. During his early years of medical practice in Sumatra, Dr. Schüffner made the discovery (1899) of the Schüffner's dots in *Plasmodium vivax*. In later years he was in charge of preventive medicine in the Netherlands Indies and then professor of tropical medicine at the Institut Colonial Royal d'Amsterdam, of which he was medical director from 1924 to 1937.

Meetings & Conferences

Feb. 17–22. American Association of School Administrators. Atlantic City, N. J.

Feb. 18–22. American Institute of Mining and Metallurgical Engineers. St. Louis.

Feb. 20–22. American Concrete Institute (Annual). San Francisco.

Feb. 21–22. American Pomological Society. Chase Hotel, St. Louis.

Feb. 22–24. American Orthopsychiatric Association. Book-Cadillac Hotel, Detroit.

Feb. 23–24. National Conference on Rural Health. Memphis, Tenn.

Feb. 26–28. Council on Industrial Health of the American Medical Association. Atlanta Biltmore, Atlanta.

Feb. 26; Mar. 5, 12, 19; Apr. 16, 23, 30. Frontiers in Chemistry Lecture Series. Science Hall, Wayne University, Detroit.

Feb. 27–Mar. 5. Paris Agricultural Show. Parc des Expositions, Porte de Versailles.

Feb. 28. Inter-Society Color Council. Wardman Park Hotel, Washington, D. C.

Mar. 1–3. Optical Society of America. Wardman Park Hotel, Washington, D. C.

Mar. 1–3. American Academy of Forensic Sciences (Annual). The Drake, Chicago.

Mar. 5–7. Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy. William Penn Hotel, Pittsburgh, Pa.

Mar. 6–8. American Mosquito Control Association (Annual). The Drake, Chicago.

Mar. 7–10. National Association for Nursery Education. Hotel Commodore, New York.

Mar. 8–9. Eastern Regional Meeting of the Institute of Navigation. Shoreham Hotel, Washington, D. C.

Mar. 11–14. American Institute of Chemical Engineers. The Greenbrier, White Sulphur Springs, W. Va.

Mar. 12–14. National Conference on Chronic Disease: Preventive Aspects. Edgewater Beach Hotel, Chicago.

Mar. 13–16. National Association of Corrosion Engineers. Hotel Statler, New York.

Mar. 15. First Congress of World Meteorological Organization. Paris.

Mar. 15–17. American Society of Tool Engineers. Hotel New Yorker, New York.

Mar. 16. Institute of the Aeronautical Sciences (Annual Flight Propulsion Meeting). Hotel Carter, Cleveland.

Mar. 16. American Ceramic Society, Pittsburgh, Pa.

Mar. 18–22. Association of American Geographers. Palmer House, Chicago.

Mar. 19–20. Histochemical Society. Detroit, Mich.

Mar. 19–23. Seventh Western Metal Exposition. Auditorium and Exposition Hall, Oakland, Cal.

Mar. 21–23. American Association of Anatomists. Detroit.

Mar. 22–24. Michigan Academy of Science, Arts and Letters. Michigan State College, East Lansing.

Mar. 23–24. Southern Society for Philosophy and Psychology. Hotel Roanoke, Roanoke, Va.

Mar. 26–29. American College Personnel Association. Stevens Hotel, Chicago.

Mar. 29–31. Congress of the Ophthalmological Society of the United Kingdom (Annual). London.

Mar. 29–31. Minnesota Section, American Chemical Society, Symposium on "Chemistry and Functions of Proteins." Natural History Museum, University of Minnesota.

The MARKET PLACE

LANGUAGES

PROFESSIONAL SERVICES

SUPPLIES AND EQUIPMENT

The MARKET PLACE

SUPPLIES AND EQUIPMENT